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PAULA DE MENDOZA BONMATÍ

Design and Synthesis of New Polyaromatic Scaffolds for Nano-Scale Applications

TESIS DOCTORAL

dirigida por Antonio M. Echavarren

Departamento
de Química Analítica i Química Orgànica

Tarragona
Abril 2010

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El Professor Dr. ANTONIO M. ECHAVARREN, Catedràtic de la Universidad Autònoma de Madrid en comissió de serveis a la Universitat Rovira i Virgili, i Group Leader a l'Institut Català d'Investigació Química,

CERTIFICA:

Que la memòria que porta per títol "Design and Synthesis of New Aromatic Scaffolds for Nano-Scale Applications", que presenta la Sra. Paula de Mendoza Bonmatí per obtenir el grau de Doctora en Química, ha estat realitzada sota la meva direcció en el meu grup de recerca a l'Institut Català d'Investigació Química.

Tarragona, Abril 2010

Prof. Dr. Antonio M. Echavarren

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A los que, aún en la distancia,
Siempre me acompañan

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Mephistopheles:

"Wo so ein Köpfchen keinen Ausgang sieht,
Stellt er sich gleich das Ende vor.
Es lebe, wer sich tapfer hält!"

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Este trabajo de investigación ha sido realizado en el Institut Català d'Investigació Química (ICIQ) bajo la dirección del Profesor Antonio M. Echavarren, a quien agradezco el haberme dado la oportunidad de formarme en su grupo, todas sus enseñanzas, paciencia, y dedicación.

Durante la realización de mi Tesis Doctoral he disfrutado de una beca financiada por la Unión Europea dentro del programa IST-FET, asociada al proyecto Pico-Inside (FP6-015847). También he participado en el proyecto NAN2004-0881-C02-02, financiado por el Ministerio de Educación y Ciencias. Quisiera agradecer a todos los participantes de ambos proyectos el descubrirme el "mundo Nano", pequeño en escala pero inmenso en espacio. En particular quisiera agradecer a los grupos del Dr. Christian Joachim, del Dr. Ernst Meyers, y del Dr. Roberto Otero, por mostrarme y tratar de hacerme comprender como "jugar" con algunas de nuestras moléculas.

Además, durante mi Tesis Doctoral, he realizado una estancia de tres meses, gracias a una beca BE de l'AGAUR, en el grupo de Murakami Sensei (Kyoto University, septiembre-octubre 2008). Me gustaría agradecer a Murakami Sensei, a Miura Sensei y a todos los miembros del grupo, su grata acogida y el haberme dado la oportunidad de ser una さん más. ありがとうございます.

En cuanto a mi trabajo en Tarragona, quisiera agradecer a todas aquellas personas que me han hecho creer que las únicos problemas por resolver se encontraban dentro de la vitrina, haciendo que mi trabajo diario resultase mucho más sencillo. En especial quisiera agradecer a nuestra coordinadora, y mucho más del grupo, Sónia Gavaldà, que tanto hace por todos y que tanto ha hecho por mí, y a nuestra técnico Vanessa Martínez quien en tantas ocasiones ha escuchado pacientemente mis quejas y solventado mis problemas. También quisiera agradecer a los servicios de soporte a la investigación del ICIQ: Al Dr. Jonathan Barr, a Joan Sallés, a Alba González y, en especial, a la Dra. Noemí Cabello, por todas las muestras que me ha "maldicido", en el servicio de espectrometría de masas y, al Dr. Gabriel González y a Kerman Gómez del servicio de RMN.

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A mis compañeros de laboratorio, quisiera agradecer a todos y cada uno de ellos, su colaboración, disponibilidad y amistad. En especial, a aquellos que han participado directamente en este trabajo: a mis amigos y mentores Dr. Domingo García-Cuadrado, Dra. Catelijne Amijs, Dr. Sergio Pascual, y Dr. Thorsten Lauterbach por transmitirme sus conocimientos y experiencias, y a José Antonio Blanco, "pequeño saltamontes", por algo similar.

Durante estos años he tenido la oportunidad de compartir el trabajo y el laboratorio con muchos otros compañeros a quienes también agradezco su presencia y buen humor diarios en el laboratorio. A los que me han sufrido más de cerca: Dra. Christelle Claverie (hasta el gato hemos compartido), Eloísa Jiménez Nuñez (compartiendo caos y amistad), Elena Herrero y Cati Ferrer (mis referentes; ellas siempre ayudándome y enseñándome el camino), Patricia Pérez (por "ese" final; merci), Mihai Raducan y Verónica López (todo, siempre y desde el principio; ahora vosotros), Dr. Antonio Rosellón (complicidad) Dr. Kian Molawi (el empate de entropía y triunfo de entalpía). También: al Dr. Dirk Spiegel, Dr. Francesco Camponovo y Anthony Pitaval (mis chicos Delta; sabéis que tengo debilidad por Manolo), a Almudena Díaz, Cristina Nieto-Oberhuber, Dra. Salomé López y Susana Porcel (las maestras pacientes y experimentadas de mis inicios), Dra. Cristina Rodríguez, Dr. Christophe Bour, y Dr. Dominic Janssen (PostDoc's que tanta energía y experiencias nos han aportado), Ana Escribano, Nicolas Delpont, César Rogelio Solorio, Claudia de León, Núria Huget Madeleine Livendahl y ... Maria Kirilova (el relevo de los joven), Dr. Julien Ceccon, Dra. Nolween Martín, Dr. José Maria Blasco y Dr. Vincent Coeffard (el relevo experimentado).

Finalmente quiero agradecer a mi familia y amigos su apoyo y cariño: a Diego y Mónica por tantas idas y venidas, a mi consiglieri, a Pau y Ainara que tanto me cuidan y hacen creer en mi misma, al "artista" de la portada, a mi madre y mi hermana por todo eso y mucho más; siempre incondicionales. Y al "fresón" que dice haber sufrido más mi tesis que mi gato.

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Hasta el momento de redactar esta memoria, los resultados aquí descritos han dado lugar a las siguientes publicaciones:

"Functionalized organic molecules: Adsorption and diffusion of single molecules on the KBr surface"

B. Such, T. Trevethan, T. Glatzel, S. Kawai, L. Zimmerli, E. Meyer, A. L. Shluger, C. H. M. Amijs, P. de Mendoza, and A. M. Echavarren, *ACS Nano*, nn-2010-00424g.

"Mechanistic Aspects of Transition Metal-Catalyzed Direct Arylation Reactions"

P. de Mendoza, and A. M. Echavarren, *Modern Arylation Methods;* Lutz Ackermann, (ed.), Wiley-VCH: Weinheim, **2009**. *Chapter 11*.

"Palladium Catalyzed Arylation for the Synthesis of Polyarenes"

S. Pascual, P. de Mendoza, and A. M. Echavarren, *Org. Biomol. Chem*. **2007**, *5*, 2727-2734.

"Bidentate Phosphines as Ligands in the Palladium-Catalyzed Intramolecular Arylation: the Intermolecular Base-Assisted Proton Abstraction Mechanism"

S. Pascual, P. de Mendoza A. C. C. Braga, F. Maseras, and A. M. Echavarren, *Tetrahedron*, **2008**, *64*, 6021-6029.

"Proton Abstraction Mechanism in the Palladium-Catalyzed Intramolecular Arylation: Substituent Effects"

D. García-Cuadrado, P. de Mendoza, A. A. C. Braga, F. Maseras, and A. M. Echavarren, *J. Am. Chem. Soc.* **2007**, *129*, 6880-6886.

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Otras publicaciones que no constan en este trabajo pero en las cuáles también he participado y han contribuido a mi formación son:

"Synthesis of Arenes and Heteroarenes by Friedel-Crafts-type Processes Catalyzed by Electrophilic Metal Complexes"

P. de Mendoza, and A. M. Echavarren*, Pure Appl. Chem*., PAC-CON-09-10-06.

"Rhodium-Catalyzed Reaction of Alkynyl Oxiranes with Arylboronic Acids Stereoselectively Produces syn-Configured a-Allenols"

T. Miura, M. Shimada, P. de Mendoza, C. Deutsch, N. Krause, and M. Murakami, *J. Org. Chem.* **2009**, *74*, 6050-6054.

"Molecular Conformation, Organizational Chirality, and Iron Metalation of meso-Tetramesitylporphyrins on Copper (100)"

D. Écija, M. Trelka, C. Urban, P. de Mendoza, E. Mateo-Martí, C. Rogero, J. A. Martín-Gago, A. M. Echavarren, R. Otero, J. M. Gallego, and R. Miranda, *J. Phys. Chem. C*, **2008**, *112*, 8988-8994.

"Templated Growth of an Ordered Array of Organic Bidimensional Mesopores"

D. Écija, M. Trelka, C. Urban, P. de Mendoza, A. M. Echavarren, R. Otero, J. M. Gallego, and R. Miranda, *Appl. Phys. Lett.* **2008**, *92*, 223117-223123.

"15-Membered Triolefinic Macrocycles as Stabilizers of Palladium(0) Nanoparticles"

Serra-Muns, R. Soler, E. Badetti, P. de Mendoza, M. Moreno-Mañas, R. Pleixats, R. M. Sebastián, and A. Vallribera, *New J. Chem.* **2006**, *30*, 1584-1594.

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Prólogo

Esta memoria del trabajo de Tesis Doctoral se ha dividido en tres partes: una introducción general que recoge brevemente las propiedades y características de los hidrocarburos policíclicos aromáticos y su aplicación en materiales moleculares, y dos capítulos independientes que constan a su vez, de una introducción, un apartado de resultados y discusión y de unas conclusiones, dónde se analizan los resultados obtenidos.

El primero de los capítulos se centra en el estudio de la reacción de arilación directa catalizada por paladio y su aplicación en la síntesis de hidrocarburos policíclicos aromáticos, tal y como se muestra en la introducción de este capítulo. En primer lugar, y continuando el trabajo realizado por el Dr. Domingo García-Cuadrado, se incluyen los estudios mecanísticos de la reacción de arilación directa que han dado lugar a una nueva propuesta sobre el mecanismo que transcurre en esta transformación. A continuación, se presentan los resultados obtenidos en colaboración con el Dr. Sergio Pascual, sobre los estudios de optimización de la reacción de arilación y su aplicación el la síntesis de nuevos hidrocarburos policíclicos aromáticos.

En el segundo capítulo se presenta el trabajo realizado dentro del proyecto Pico-Inside sobre el diseño y la síntesis de nuevos dispositivos moleculares electrónicos capaces de actuar como puertas lógicas. En particular, nos hemos centrado en la síntesis de dos familias de moléculas con tres extremidades poliaromáticas: los truxenes, cuyo diseño y preparación se ha llevado a cabo en colaboración con la Dra. Catelijne Amijs, y los starfenos. En cuanto a la síntesis de starfenos se han diseñado varias rutas sintéticas divergentes, la primera de ellas también se ha llevado a cabo en colaboración con la Dra. Catelijne Amijs, mientras qua la síntesis de la molécula decastarpheno se ha realizado en colaboración con el Dr. Thorsten Lauterbach. Dentro de este poyecto también se han realizado estudios en colaboración con José Antonio Blanco para la síntesis de la molécula tetraceno[2,3,*l*]-nonafeno, pero debido a los resultados todavía preliminares no se incluyen en esta memoria. Para finalizar este capítulo se han incluido

algunos de los trabajos realizados por nuestros colegas del proyecto Pico-Inside sobre la visualización y manipulación de algunas de las moléculas preparadas y sus aplicaciones potenciales en nuevos dispositivos electrónicos.

A lo largo de esta tesis también se ha participado en el proyecto *Biomimetic Model Systems of Surface Processes* (NAN2004-0881-C02-02), cuyos resultados, por tratar de sistemas distintos, tampoco se incluyen en la presente memoria.

Por último, en este manuscrito las abreviaciones y acrónimos utilizados comúnmente en química orgánica y organometálica han sido empleados siguiendo las recomendaciones de "Guidelines for authors" *J. Org. Chem*. **2007**, *70*, 13A-27A.

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Resumen

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Design and Synthesis of New Polyaromatic Scaffolds for Nano-Scale Applications

Los hidrocarburos policíclicos aromáticos (HPAs) son una amplia clase de moléculas orgánicas constituidas por anillos aromáticos fusionados. El descubrimiento en los años 70 sobre las propiedades conductoras y semiconductoras de los polímeros orgánicos conjugados[1] y, además, el descubrimiento en 1985 de la molécula C_{60} fullereno,[2] significaron un creciente interés en la síntesis de nuevos HPAs[3] y en su aplicación en dispositivos moleculares electrónicos y optoelectrónicos. [4]

Arilación Directa Catalizada por Paladio: Estudios Mecanísticos y su Aplicación en la Síntesis de HPAs.

La reacción intramolecular de arilación directa catalizada por paladio se trata de un método directo para la formación de compuestos carbo- y heterocíclicos y por tanto apropiado para la síntesis de HPAs. A diferencia de las ampliamente estudias reacciones de acoplamiento cruzado en las que se utilizan precursores organometálicos, el mecanismo que opera en las reacciones de arilación directa de arenos, resulta menos conocido.

Como parte de mi trabajo de investigación, hemos estudiado la regioselectividad en la reacción intramolecular catalizada por paladio de bromodiarilmetanos **1** que incorporan varios sustituyentes en diferentes posiciones de uno de los anillos aromáticos. Tras la reacción catalítica, se observa como grupos electro-atrayentes en posición ortho respecto a enlace C-H que se activa, como por ejemplo, fluoruros, cloruros o

---

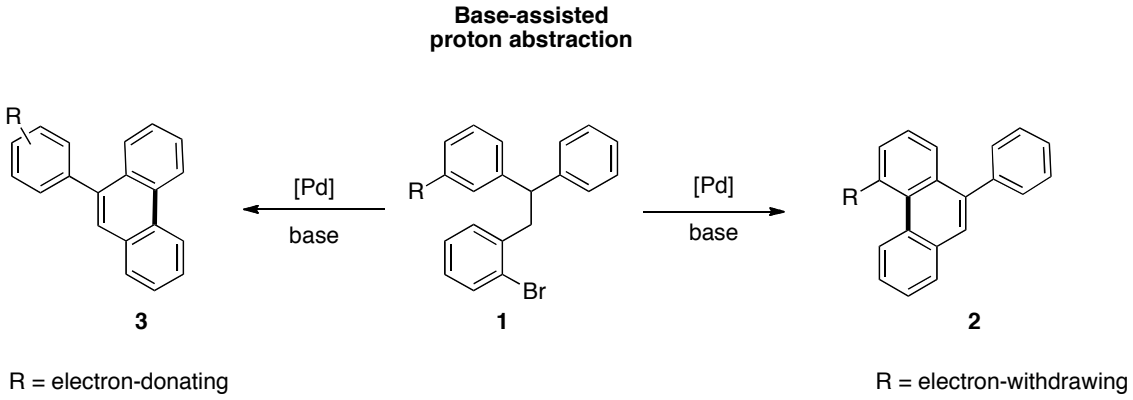
1 See nobel prize lectures: (a) Shirakawa, H. *Angew. Chem. Int. Ed*. **2001**, *40*, 2574. (b) MacDiarmid, *Angew. Chem. Int. Ed*. **2001**, *40*, 2581. (c) Heeger, A. J. *Angew. Chem. Int. Ed*. **2001**, *40*, 2591.

2 Kroto, H. W.; Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. *Nature* **1985**, *318*, 162.

3 (a) Scott, L. T. *Angew. Chem. Int. Ed.* **2004**, *43*, 4994-5007. (b) Pascual, S., de Mendoza, P., Echavarren, A. M. *Org. Biol. Chem.* **2007**, *5*, 2727.

4 Anthony, J. E. *Agew. Chem. Int. Ed.* **2008**, *47*, 452.

trifluorometilos, favorecen la reacción en el anillo substituido, mientras que los grupos en posición para muestran un regioselectividad moderada, **2**. Por otro lado, grupos electro-dadores como *tert*-butilos o trimetilsililos, dirigen la reacción hacia el anillo no sustituido, **3** (*Esquema 1*).



Esquema 1

De acuerdo con los datos experimentales, estudios computacionales muestran como ésta reacción transcurre a través de un mecanismo que implica la abstracción de un protón por medio de una base. Estos resultados, son inconsistentes con el previamente propuesto mecanismo de sustitución electrófila aromática, generalmente asumido para esta transformación.[5]

A continuación, una vez establecida la nueva propuesta mecanística, procedimos a optimizar la reacción de arilación directa, con el objetivo de aplicar la reacción en la síntesis de nuevos hidrocarburos policíclicos de aromaticidad extendida y fullerenos aplastados.[6] Así, utilizando las condiciones más efectivas previamente encontradas, pudimos llevar a cabo la formación de seis enlaces carbono-carbono, e in situ

5 (a) García-Cuadrado, D.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem Soc.* **2006**, *128*, 1066. (b) García-Cuadrado, D.; de Mendoza, P.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem Soc.* **2007**, *129*, 6880.

6. Pascual, S.; de Mendoza, P. Ataualpa, Braga, A. C.; Maseras, F.; Echavarren, A. M. *Tetrahedron* **2008**, *64*, 6021.

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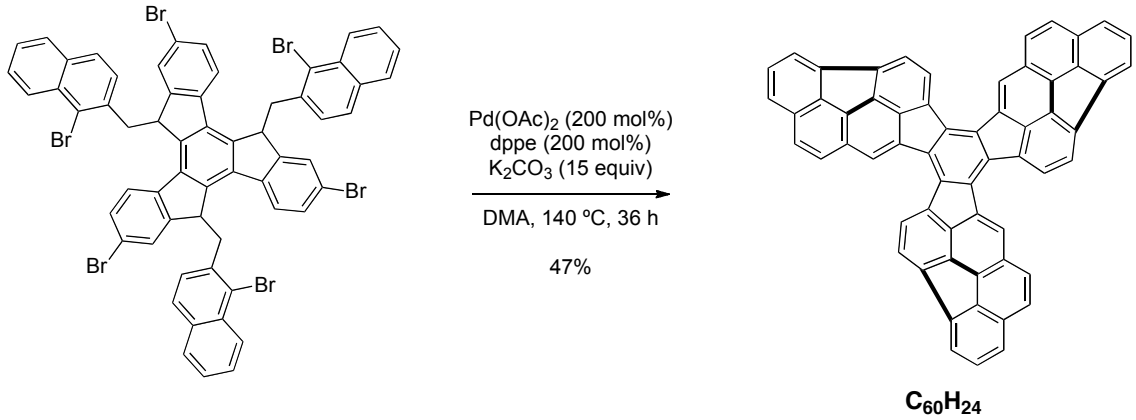
deshydrogenación, en una sola etapa para la síntesis de la molécula $C_{60}H_{24}$ (*Esquema 2*).



Esquema 2

Conmutando Dentro de Una Única Molécula

La electrónica molecular[7] se basa en el uso de moléculas orgánicas, capaces de desempeñar funciones electrónicas básicas, como unidades elementales para la construcción de circuitos integrados mediante la aproximación denominada "de abajo-a-arriba". Por ello, el diseño, la síntesis, el ensamblaje y el control de sistemas moleculares electrónicos resultan desafíos cruciales en el campo de la nanotecnología.

Pico-Inside*,* es un proyecto integrado financiado por la Unión Europea, cuyo objetivo es llevar a cabo cálculos dentro de una única molécula utilizando nueva tecnología a escala atómica.[8] Nuestra participación en el proyecto consiste en el diseño y la síntesis de sistemas poliaromáticos con tres brazos, que puedan ser aplicados como *puertas lógicas* en circuitos intramoleculares integrados.

Para ello hemos desarrollado aproximaciones divergentes para la síntesis de moléculas aromáticas en forma de Y, que previamente han sido diseñadas como candidatas para su

7 (a) Joachim, C. Gimzewski, J. K. Aviram. A. *Nature*, **2000**, *408*, 541. (b) Jlidat, N. Hilwa, M. Joachim, C. *Chem. Phys. Lett*. **2009**, *470*, 275.

8 Gourdon, A. *NanoLetters* **2006**, *4*, 22.

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posterior aplicación como unidades conmutadoras. En particular, hemos preparado una serie de moléculas derivadas del truxeno siguiendo la metodología desarrollada en nuestro grupo de investigación[9] y hemos explorado nuevas estrategias para la obtención de otra clase de moléculas poliaromáticas pertenecientes a la familia de los starfenos y sus derivados.

Además, estudios preliminares por parte de otros participantes del proyecto Pico-Inside,[10] como el depositar las moléculas en superficies aislantes, imágenes de STM y medidas relacionadas con el proceso de transporte electrónico intramolecular, han sido llevados a cabo con el fin de investigar las propiedades de estas subunidades orgánicas hacia la implantación en dispositivos electrónicos reales (ver *Ilustración 1* a modo de ejemplo).

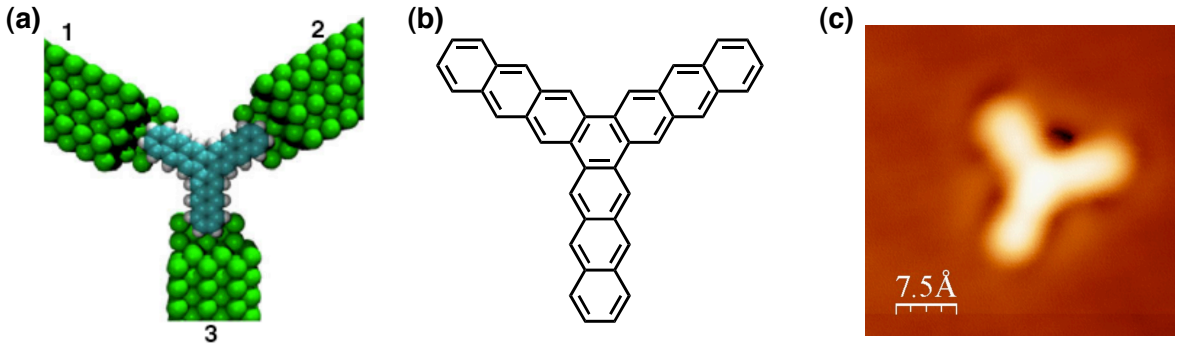

Ilustración 1: (a) Diseño, (b) síntesis e (c) imágenes LT-UHV-STM de la molécula dianthra[a,c]naphthaceno.

9 (a) de Frutos, Ó.; Gómez-Lor, B.; Granier, T.; Monge, M. Á.; Gutiérrez-Puebla, E.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **1999**, *38*, 204-207. (b) Gómez-Lor, B.; de Frutos, Ó.; Ceballos, P. A.; Granier, T.; Echavarren, A. M. *Eur. J. Org. Chem.* **2001**, 2107-2114. (c) Gómez-Lor, B.; González-Cantalapiedra, E.; Ruiz, M.; de Frutos, Ó.; Cárdenas, D. J.; Santos, A.; Echavarren, A. M. *Chem. Eur. J.* **2004**, *10*, 2601-2608.

10 Christian Joachim's research group at the CMES/CNRS: *Centre d'Elaboration des Matériaux et d'Etudes Structurales* in Toulouse, France.

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Introduction

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Introduction:

Polycyclic Aromatic Hydrocarbons in Molecular Materials

There's Plenty of Room at the Bottom is the title of the classic lecture given by the Nobel laureate physicist Richard Feynman in 1959.[11] In his talk, Feynman discussed the possibilities, advantages, and challenges of governing elements on the nanometric scale. He noted many different ways the world could be improved through the development of small-scale technology, such as miniaturized and faster computers, together with the possible advances in life sciences. Feynman considered no physical limitations for arranging atoms the way one wants and therefore, he considered the possibility of direct manipulation of individual discrete atoms as a complementary tool for synthetic chemistry. However, he recognized the technological limitations at that time and he particularly encouraged young scientists in the development of more powerful computers and microscopes, which would allow observation and manipulation at a much smaller scale. His peroration has since then been referred to as the defining moment of nanotechnology.

Some of the ideas Feynman exposed in 1959 have been later achieved and nanotechnology is nowadays one of the major interdisciplinary areas of research in modern science. Unambiguously, one of the most important milestones in the field was the development of modern scanning probe techniques such as the scanning tunneling microscope (STM) at the beginning of the 1980's.[12] This is especially suited for studying the structure of adsorbed molecules on surfaces and for probing their electronic properties at the atomic scale.[13] Since then, a revolution in the real-space imaging and manipulation of atoms and molecules have given rise to a new field in

11 Lecture delivered on December 29th at the annual meeting of the American Physical Society at California Institute of Technology and first published in February 1960: Feynman R. P. *Eng. Sci.* **1960**, *23*, 22-36. (http://www.zyvex.com/nanotech/feynman.html).

12 Binning, G.; Rohrer, H.; Gerber, Ch.; Weibel, E. *Phys. Rev. Lett.* **1982**, *49*, 57-61.

13 Rabe, J. P.; Buchholz, S. *Science* **1991**, *253*, 424-427.

molecular science, where the fully understanding and control of molecules in the nanometer scale is a major challenge in order to envision future applications in organic molecular materials like molecular electronic devices.

A main characteristic in organic materials is that molecular properties at the nano-scale may differ considerably from the fundamental properties governing in the micro or the macro world. For instance, quantum effects may control electronic, magnetic or optical physical properties, enabling molecular materials exclusive potential applications. Furthermore, molecules offer the possibility to customize materials with pre-designed properties by synthetically modifying their molecular structure and functionalities according to their future target applications.

A highly attractive class of compounds with potential applications in the field of organic materials are polycyclic aromatic hydrocarbons (PAHs) constituted by fused aromatic rings. Aromatic compounds are mainly characterized by their delocalized π-electrons that provide them unique properties on the molecular scale. Nonetheless, despite the frequent use of terms like aromatic and aromaticity, these have no precise meaning and do not directly refer to any measurable property. Thus, although it is generally accepted that aromatic hydrocarbons are cyclic and fully conjugated systems that possess delocalized π-electrons, different criteria like reactivity,[14] thermodynamic[15] and spectroscopic properties[16] have been used to introduce indices of aromaticity.[17]

Since Faraday's isolation of benzene in 1825,[18] where its empirical *formula* (CH) indicated a high degree of unsaturation and experimentally presented lower and different reactivity than olefins, many chemists tried to find the actual structure of this main aromatic compound. In 1865, Kekulé postulated the "oscillating" 1,3,5-

14 Shaik, S.; Shurki, A.; Danovich, D.; Hiberty, P. C. *Chem. Rev*. **2001**, *101*,1501-1540.

15 Slayden, S.; Liebman, J. F. *Chem. Rev*. **2001**, *101*, 1541-1566.

16 Reginald H.; Mitchell, R. H. *Chem. Rev*. **2001**, *101*, 1301-1316.

17 For detailed review studies see special issue on *Aromaticity*: Schleyer, P. v. R., Ed.; *Chem. Rev*. **2001**, *101* (5).

18 Faraday, M. *Phil. Trans. R. Soc. Lond.* **1825**, *115*, 440-466.

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cyclohexatriene structure (*Figure 1*), which in contrast to other models proposed at that time, enabled to rationalize the product distribution found during substitution reaction of benzene. However, the Kekulé model failed to explain why its reactivity was so different to that of ordinary olefins for which instead of substitution, addition reactions were preferred.

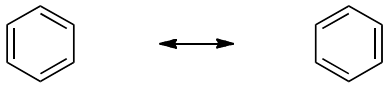

Figure 1: Kekulé's "oscillating" 1,3,5-cyclohexatriene structure for benzene.

Throughout the 19th century, the term aromaticity was employed to relate the fragrance properties of certain compounds. In the 1930's, during the development of quantum mechanics theory, Hückel proposed the first theoretical definition of aromaticity in accordance to the stability and reactivity of aromatic compounds. Based on Molecular Orbital Theory, he suggested that aromatic systems are planar cyclic hydrocarbons with $4n + 2$ delocalized π-electrons, being n an integer number.[19] Further on, many theoretical and experimental work concerning their geometric (bond order and length alternation as well as structural planarity tendency), energetic and magnetic properties have been performed in order to redefine aromaticity in terms of experimental properties.[15,14,16,17]

An alternative way to assess stability and predict reactivity of polyfused aromatic hydrocarbons is based on the localization of aromatic sextets proposed by Clar.[20] According to Clar's rule, the most stable structure of a determinate PAH is the one containing the major number of π-electron sextets. Hence, he assigned the π-electrons that can participate in aromatic sextets to specific rings, showing that aromaticity is not a molecular property but localized in distinct rings. For example, in the case of phenanthrene two structures can be drawn: one with two aromatic sextets at the

19 Hückel, E. *Z. Phys*. **1931**, *70*, 204-286.

20 Clar, E. *The Aromatic Sextet*; John Wiley & Sons: London, **1972**.

peripheral rings and a second one with a single sextet in the central benzenoid ring (see *Figure 2*). The first one, possessing two aromatic sextets, is more stable and the π-electrons at the 9,10 positions of the phenanthrene have a more double bond character and thus, undergo addition rather than substitution reactions. Theoretical calculations, including the Nucleus Independent Chemical Shift (NICS) concept have corroborated Clar's rule predicting aromatic character of different rings inside a specific polyaromatic compound.[21]

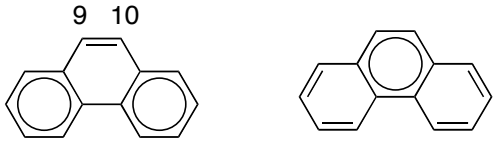

Figure 2: Clar's representation of aromatic sextets in phenanthrenes.

PAHs are ubiquitous contaminants derived mainly from incomplete combustion of fossil fuels like oil, gas coal and wood[22] that are even present in interstellar space.[23] The finding of the carcinogenic properties of benzo[*a*]pyrene and dibenz[*a*,*h*]anthracene (*Figure 3*) in the 1930's, provoke an increasing interest in the development of innovating synthetic methods for the preparation of new PAHs in order to investigate the relation between structure and toxicity.[24]

21 (a) Schleyer, P. v. R.; Maerker, C.; Dransfeld, A.; Jiao, H.; Hommes, N. J. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317-6318. (b) Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev*. **2005,** *105*, 3842-3888

22 (a) Clar, E. *Polycylic Hydrocarbons*; Academia Press: New York, **1964**; Vol. I/II. (b) Harvey, R. G. *Polycylic Aromatic Hydrocarbons*, Wiley-VCH: New York, **1997**.

23 Henning, Th.; Salama, F. *Science* **1998**, *282*, 2204-2210.

24 (a) Harvey, R. G. *Polycylic Aromatic Hydrocarbons: Chemistry and carcinogenicity;* Cambridge University Press: Cambridge, **1991**. (b) Luch, A. *The Carcinogenic Effects of Polycyclic Aromatic Hydrocarbons;* Imperial College Press: London, **2005**.

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benzo[*a*]pyrene dibenz[*a*,*h*]anthracene

Figure 3: Two representative PAHs with carcinogenic properties.

Fundamental contributions on the synthesis and characterization of new aromatic compounds were made by Scholl[25] and Clar[26] during the first half of the 20th century. Noteworthy, at that time, PAHs synthesis was still limited to small size systems under drastic conditions like high temperatures and high pressures, affording usually poor isolated yields.

The discovery in the 1970's of semiconducting and conducting properties of conjugated organic polymers[27] and, moreover, the discovery in 1985[28] of a third allotrope form of carbon, hollow cage C_{60} fullerene,[29] prompted new research interests towards the synthesis of new PAHs and their application in organic molecular devices.

Besides their delocalized π-electrons, main features in aromatic compounds are their rigid and well-defined geometric structures and, in many cases, their relatively high thermal, photochemical, and chemical inertness. All these unique characteristics and, in

25 (a) Scholl, R.; Seer, C.; Weitzenböck, R. *Chem. Ber*. **1910**, *43*, 2202-2209. (b) Scholl, R.; Seer, C. *Liebigs Ann. Chem*. **1912**, *394*, 111-123. (c) Scholl, R.; Neumann, H. *Chem. Ber*. **1922**, *55*, 118-126. (d) Scholl, R.; Seer, C. *Chem. Ber*. **1922**, *55*, 330-341.

26 (a) Clar, E. *Nature* **1948**, *161*, 238-239. (b) Clar, E. *Chem. Ber.-Recl*. **1948**, *81*, 52-63. (c) Clar, E. *Chem. Ber.-Recl.* **1949**, *82*, 495-514. (d) Clar, E.; Stewart, D. G. *J. Am. Chem. Soc*. **1953**, *75*, 2667-2672.

27 See Nobel prize lectures: (a) Shirakawa, H. *Angew. Chem. Int. Ed*. **2001**, *40*, 2574-2580. (b) MacDiarmid, *Angew. Chem. Int. Ed*. **2001**, *40*, 2581-2590. (c) Heeger, A. J. *Angew. Chem. Int. Ed*. **2001**, *40*, 2591-2611.

28 Kroto, H. W.; Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. *Nature* **1985**, *318*, 162-163.

29 (a) Kroto, H. W.; Allaf, A. W.; Balm, S. P. *Chem. Rev*. **1991**, *91*, 1213-1235. (b) See special issue on *Fullerenes*: McLafferty, F. W., Ed.; *Acc. Chem. Res*. **1992**, *25* (3).

particular, their efficient charge transport due to their low HOMO-LUMO gap,[30] make them potentially useful materials[31] in organic optoelectronic devices such as light-emitting diodes, field-effect transistors, and photovoltaics.[32,33,34] Furthermore, well-defined nanostructures resulting from supramolecular self-assembly of PAHs, such as nanotubes and nanowires, have a great potential in organic materials.[35,36,37]

Tetracene and pentacene (*Figure 4*) are among the most promising molecular conductors and semiconductors for organic field-effect transistors (OFETs) based on linear acenes.[34] The oligoacene units are a basic building block of graphite[38] or carbon nanotubes.[39] Thus, studying their electronic properties is important for understanding the structure and properties of the latter materials. Due to the poor solubility and facile photo-degradation of pentacene and higher aromatic compounds,[40] appropriate substitution to assess stability and functional properties is required.[41]

Tetracene Pentacene

Figure 4: Representative acenes: tetracene and pentacene.

30 Bendikov, M.; Wudl, F.; Perepichka, D. F. *Chem. Rev.* **2004**, *104*, 4891-4945.

31 *Carbon-Rich Compounds. From Molecules to Materials*; Haley, M. M., Tykwinsli. R. R., Eds.; Wiley-VCH: Wenheim, **2006**.

32 Dimitrakopoulos, C. D.; Malenfant, P. R. L. *Adv. Mater.* **2002**, *14*, 99-117.

33 See special issue on *Organic Electronics and Optoelectronics:* Forrest, S. R., Thompson, M. E., Eds.; *Chem. Rev.* **2007**, *107* (4).

34 Anthony, J. E. *Angew. Chem. Int. Ed.* **2008**, *47*, 452-483.

35 Adachi, M.; Murata, Y.; Takao, J.; Jiu, J. T.; Sakamoto, M.; Wang, F. M. *J. Am. Chem. Soc*. **2004**, *126*, 14943-14949.

36 Law, M.; Greene, L. E.; Johnson, J. C.; Saykally, R.; Yang, P. D. *Nat. Mater*. **2005**, *4*, 455-459.

37 Zhu, K.; Neale, N. R.; Miedaner, A.; Frank, A. J. *Nano Lett*. **2007**, *7*, 69-74.

38 Chung, D. D. L. *J. Mater. Sci.* **2002**, *37*, 1475-1489.

39 Iijima, S.; Ichihashi, T. *Nature* **1993**, *363*, 603-605.

40 (a) Ono, K.; Totani, H.; Hiei, T.; Yoshino, A.; Saito, K.; Eguchi, K.; Tomura, M.; Nishida, J.; Yamashita, Y. *Tetrahedron* **2007**, *63*, 9699-9704. (b) Palayangoda, S. S.; Mondal, R.; Shah, B. K.; Neckers, D. C. *J. Org. Chem*. **2007**, *72*, 6584-6587.

41 Jiang, J.; Kaafarani, B. R.; Neckers, D. C. *J. Org. Chem.* **2006**, *71*, 2155-2158.

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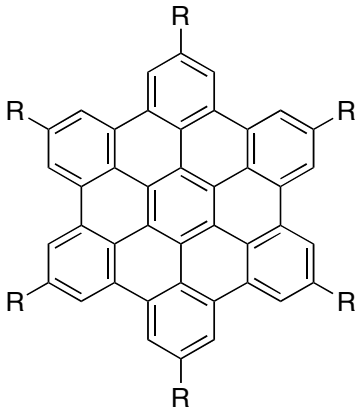
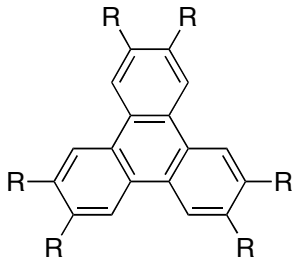
Interesting classes of non-linear acenes are discotic and star-shaped molecules with flexible peripheral chains like functionalized hexa-*peri*-hexabenzocoronene and triphenylenes (*Figure 5*). Due to π-stacking interactions between their rigid aromatic cores, they tend to self-assemble in highly ordered 2D supramolecular arrays forming columnar disk-type liquid crystals π-systems. This property makes them attractive model systems for studying their charge and energy transport for its applications in electronic devices. [42,43]



Hexa-*peri*-hexabenzocoronene



Triphenylene

Figure 5: Discotic and star-shape PAHs that can aggregate to form 2D arrays forming Liquid Crystals.

Although these graphite-like polyacenes (nanographenes) are flat, some extended PAHs tend to be distorted due to steric interactions. For example, *ortho* poly-condensed benzenoid rings like [6]-helicene adopt a helicoidal shape (*Figure 6*). Helicenes are unique 3D aromatic systems that are inherently chiral and therefore their electronic applications[44] can be combined with their chiroptical properties.[45]

42 Adam, D.; Schuhmacher, P.; Simmerer, J.; Häussling, L.; Siemensmeyer, K.; Ringsdorf, H.; Haarer, D. *Nature* **1994**, *371*, 141-143.

43 See Reviews: (a) Sergeyev, S.; Pisula, W.; Geerts, Y. H. *Chem. Soc. Rev*. **2007**, *36*, 1902-1929. (b) Wu, J.; Pisula, W.; Müllen, K. *Chem. Rev*. **2007**, *107*, 718-747.

44 (a) Katz, T. J. *Angew. Chem. Int. Ed.* **2000**, *39*, 1921-1923. (b) Rajca, A.; Miyasaka, M. In *Funcional Organic Materials. Syntheses, Strategies and Applications;* Millar, T. J. J., Bunz, U. H. F., Eds.; Wiley-VCH: Weinheim, **2007**, 547-581. (c) Sehnal, P.; Stará, I. G.; Saman, D.; Tichy M.; Mísek, J.; Cvacka, J.; Rulísek, L.; Chocholousová, J.; Vacek, J.; Goryl, G.;

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Besides, polyaromatic systems where pentagonal rings are surrounded by hexagonal rings are forced to adopt curved structures and belong, in a broader sense, to the family of fullerenes. Such bowl-shaped polyarenes[46] are characterized by a high degree of strain[47] as a result of the pyramidalization of the internal trigonal carbon atoms. For instance, corannulene (or [5]-circulene, $C_{20}H_{10}$)[48] depicted in *Figure 6* is the minimal subunit that presents curvature, and its carbon framework follows the pentagon rule inherent in C_{60} fullerene.

Figure 6: [6]-Helicene and corannulene structures.

Indeed, the existence of C_{60} fullerene, shown in *Figure 7*, was already predicted by Osawa in the 1970s,[49] as he noticed that corannulene could be a subunit of a larger C_{60} hollow spherical system. This highly symmetric ball-shaped molecule, with truncated icosahedron form, was predicted to be a stable species with interesting properties that Osawa defined as "superaromaticity".[50]

Szymonski, M.; Císarová, I.; Stary, I. *Proc. Natl. Acad. Sci.* **2009**, *106*, 13169-13174.

45 Collins, S. K.; Vachon, M. P. *Org. Biomol. Chem*. **2006**, *4*, 2518-2524.

46 Tsefrikas, V. M.; Scott, L. T. *Chem. Rev*. **2006**, *106*, 4868-4884 and references therein.

47 Kiyobayashi, T.; Nagano, Y.; Sakiyama, M.; Yamamoto, K.; Cheng, P.-C.; Scott, L. T. *J. Am. Chem. Soc.* **1995**, *117*, 3270-3271.

48 For a review on [5]-circulene see: Siegel, J. S.; Seiders, T. J. *Chem. Britain* **1995**, 313-316.

49 Osawa, E. *Kagaku* **1970**, *25*, 854-863.

50 In commemoration of the thirtieth anniversary of Osawa's C_{60} paper: Slanina, Z. *J. Mol. Graphics Modell*. **2001**, *19*, 181-184.

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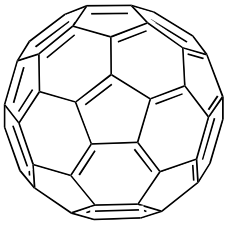

Figure 7: Fullerene C_{60} structure.

Very soon after the isolation of this fascinating molecule by Kroto *et al.*,[29] fullerene C_{60} and its charge-transfer salts were demonstrated to be promising electronic materials. Among the most spectacular physical and chemical properties, C_{60} was found to behave as a strongly electron-accepting molecule. It is able to reversibly accept up to six negative charges, showing exceptional electronic absorption bands expanding throughout the entire UV-Vis spectrum, displaying a strong singlet oxygen sensitizing ability, and featuring interesting non-linear optical properties.[51,52,53,54]

Although C_{60} is the most abundant and well-characterized member of the fullerene family, a considerable number of higher (C_{70}, C_{76}, C_{84}, C_{90}, C_{94} …)[55] or even lower ($C_{50}Cl_{10}$)[56] fullerenes have also been detected or isolated. All of them, including

51 (a) Echegoyen, L.; Diederich F.; Echegoyen, L. E. In *Electrochemistry of Fullerenes*; Kadish, K. M., Ruoff, R. S., Eds.; Wiley Interscience: New York, **2000.** (b) Echegoyen, L.; Echegoyen, L. E. In *The Electrochemistry of C_{60} and Related Compounds*; Henning, L., Hammerich, O., Eds.; Marcel Dekker: New York, **2001.** (c) Armaroli, N. In *Photoinduced Energy Transfer Processes in Functionalized Fullerenes*; Guldi, D. M., Martín, N., Eds.; Kluwer Academic: Dordrecht, **2002**.

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56 Xie, S. Y.; Gao, F.; Lu, X.; Huang, R. B.; Wang, C. R.; Zhang, X.; Liu, M. L.; Deng, S. L.; Zheng, L. S. *Science* **2004**, *304*, 699-699.

cylindrical nanotube fullerenes,[57] present extraordinary electronic properties and are promising candidates for molecular material devices.

Fullerenes C_{60} and C_{70} can be readily produced via vaporization of graphite in an electric arc in the presence of an inert quenching gas atmosphere (He).[58] However, this methodology is not efficient for producing large amounts of C_{60}, C_{70}, or higher fullerenes and cannot be applied for the preparation of pre-designed fullerenes like endohedral fullerene complexes or heterofullerenes. These drawbacks render the production of this molecule by conventional synthetic methods a great challenge. Despite many efforts, rational syntheses of any of the respective fullerenes from unimolecular precursor still remain elusive in a large amount scale. Among the most promising candidates for a total synthesis of fullerenes[59,60,61] are bowl-shaped aromatic hydrocarbons.[62,63,64,65]

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57 Yang, H.; Beavers, C. M.; Wang, Z.; Jiang, A.; Liu, Z.; Jin, H.; Mercado, B. Q.; Olmstead, M. M.; Balch A. L. *Angew. Chem. Int. Ed*. **2010**, *49*, 886-890.

58 Krätschmer, W.; Lamb, L. D.; Fostiropoulos, K.; Fuman, D. R. *Nature* **1990**, *347*, 354-358.

59 Diederich, F.; Rubin, Y. *Angew. Chem. Int. Ed.* **1992**, *31*, 1101-1264.

60 Rubin, Y. *Chem. Eur. J.* **1997**, *3*, 1009-1016.

61 The obtention of mass peak corresponding to $C_{60}^{+\cdot}$ has been reported from cyclic polyynes: (a) Tobe, Y.; Nakagawa, N.; Naemura, K.; Wakabayashi, T.; Shida, T.; Achiba, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4544-4545. (b) Rubin, Y.; Parker, T. C.; Pastor, S. J.; Jalisatgi, S.; Boulle, C.; Wilkins, C. L. *Angew. Chem. Int. Ed.* **1998**, *37*, 1226-1229.

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Even though progresses in modern synthetic methods and analytical techniques have enabled the selective synthesis of a broad range of new PAHs with different sizes and shapes under milder conditions in the last years,[66] their preparation is often impeded by low reaction efficiency and the poor solubility of the resulting aromatic systems, which difficult their isolation and characterization. Therefore, the synthesis of extended PAHs still remains a extremely high challenging task.

66 Hagen, S.; Hopf, H. *Top. Curr. Chem*. **1998**, *196*, 44-89. (b) See special issue on *Novel Aromatic Compounds*: Scott, L. T., Siegel, J. S., Eds.; *Tetrahedron* **2001**, *57* (17). (c) Harvey, R. G. *Curr. Org. Chem*. **2004**, *8*, 303-323.

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Chapter I

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Chapter I:

Palladium-Catalyzed Direct Arylation Reactions

1. Introduction

Biaryls and polyarenes are key structures present in a wide variety of functional organic materials.[67] Their formation generally relies on transition metal catalyzed cross-coupling reaction[68,69,70] between aryl halides, or their synthetic equivalents like aryl triflates, and organometallic reagents. Noteworthy, preactivation of both aryl moieties usually requires additional time-consuming synthetic steps, generating wastes from reagents, solvents, and purification methods. Besides, cross-coupling reactions with both functionalized aryls produces stoichiometric organometallic by-products, making the transformation neither atom economical nor environmentally friendly. A more ecologically benign and economically attractive alternative is the metal-catalyzed direct arylation reaction,[71] where one of the functionalized aryls is replaced with a non-activated arene. The reaction proceeds via C-H bond activation, reducing considerably the by-products and wastes generated during this transformation (*Scheme 1*).

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67 Anthony, J. E. *Angew. Chem. Int. Ed.* **2008**, *47*, 452-483.

68 *Metal-Catalyzed Cross-Coupling Reactions*, de Meijere, A., Diederich, F., Eds; Wiley-VCH: Weinheim, **2004**.

69 Special issue on *Cross-Coupling Reactions*: Buchwald, S. L., Ed.; *Acc. Chem. Res*. **2008**, *41* (11).

70 For recent selected reviews on *Cross-Coupling Reactions*: (a) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev*. **2002**, *102*, 1359-1469. (b) Corbet, J. P.; Mignani, G. *Chem. Rev*. **2006**, *106*, 2651-2710. (c) Roglans, A.; Pla-Quintana, A.; Moreno-Mañas, M. *Chem. Rev*. **2006**, *106*, 4622-4643, and references therein.

71 For recent selected reviews on *Direct Arylation Reactions*: (a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174-238. (b) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev*. **2007**, *36*, 1173-1193. (c) Campeau, L.-C.; Stuart, D. R.; Fagnou, K. *Aldrichimica Acta* **2007**, *40*, 35-41. (d) Campeau, L.-C.; Fagnou, K. *Chem. Soc. Rev.* **2007**, *36*, 1058-1068. (e) Pascual, S.; de Mendoza, P.; Echavarren, A. M. *Org. Biol. Chem.* **2007**, *5*, 2727-2734. (f) Catellani, M.; Motti, E.; Della Ca', N.; Ferraccioli, R. *Eur. J. Org. Chem.* **2007**, *25*, 4153-4165. (g) Li, B.-J.; Yang, S.-D.; Shi, Z.-J. *Synlett* **2008**, *7*, 949-957. (h) McGlacken, G. P.; Bateman, L. M. *Chem. Soc. Rev*. **2009**, *38*, 2447-2464. (i) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem. Int. Ed*. **2009**, *48*, 5094-5115. (j) Kulkarni, A. A.; Daugulis, O. *Synthesis* **2009**, *24*, 4087-4109. (k) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew.*

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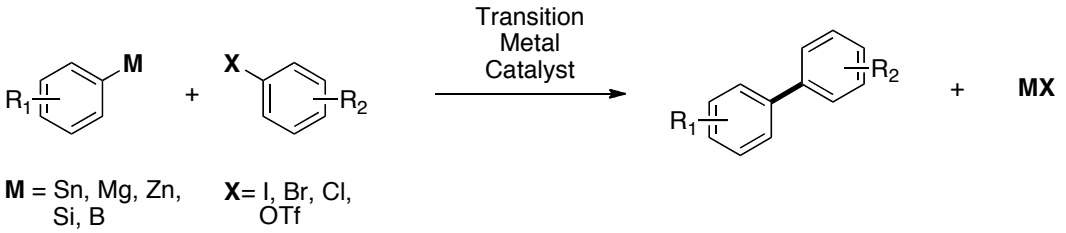
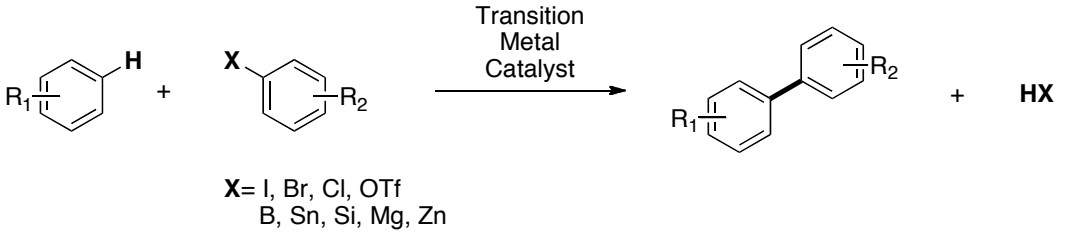
Cross-Coupling Reactions



Direct Arylation with Unactivated Aryls



Scheme 1

Although cross-coupling methods, in particular those based on the use of palladium or nickel catalysts such as the Suzuki-Miyaura,[72] Stille,[73,74] Negishi,[75] and Sonogashira[76] couplings still dominate the synthetic arena, increasingly attention is being paid in the use of direct arylation reactions for the synthesis of complex natural products[71a,77] and polyarenes.[71e,78,79]

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72 See review: Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457-2483.

73 Stille, J. K. *Angew. Chem. Int. Ed.* **1986**, *25*, 508-524.

74 See reviews: Espinet, P.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 4704-4734. (b) *Tin Chemistry*, Davies, A. G., Gielen, M., Pannell, K. H., Tiekink, E. R. T., Eds.; Wiley-VCH: Wenheim **2008**, 561-578.

75 See review: Negishi, E.; Huang, Z.; Wang, G.; Mohan, S.; Wang, C.; Hattori, H. *Acc. Chem. Res*. **2008**, *41*, 1474-1485.

76 Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627-630.

77 See selected examples: (a) Abe, H.; Takeda, S.; Fujita, T.; Nishioka, K.; Takeuchi, Y.; Harayama, T. *Tetrahedron Lett.* **2004**, *45*, 2327-2329. (b) Torres, J. C.; Pinto, A. C.; Garden, S. J. *Tetrahedron* **2004**, *60*, 9889-9900. (c) Harrowven, D. C.; Woodcock, T.; Howes, P. D. *Angew. Chem. Int. Ed.* **2005**, *44*, 3899-3901. (d) Bowie, A. L.; Hughes, C. C.; Trauner, D. *Org. Lett.* **2005**, *7*, 5207-5209. (e) Ackermann, L.; Althammer, A. *Angew. Chem. Int. Ed.* **2007**, *46*, 1627-1629. (f) Bedford, R. B.; Betham, M. *J. Org. Chem.* **2006**, *71*, 9403-9410. (g) Tamiya, M.; Ohmori, K.; Kitamura, M.; Kato, H.; Arai, T.; Oorui, M.; Suzuki, K. *Chem. Eur. J.* **2007**, *13*, 9791-9823.

78 Echavarren, A. M.; Gómez-Lor, B.; González, J. J.; de Frutos, Ó. *Synlett* **2003**, 585-597.

79 (a) Wu, Y.-T.; Siegel, J. S. *Chem. Rev.* **2006**, *106*, 4843-4867. (b) Tsefrikas, V. M.; Scott, L.

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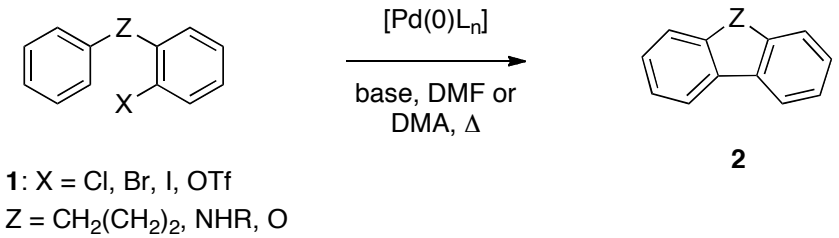
1.1 Synthesis of Large Polyarenes via Palladium-Catalyzed Direct Arylation

The intramolecular palladium-catalyzed direct arylation has been demonstrated to be synthetically highly useful for the transformation of low-functionalized compounds **1** to form carbo- and heterocycles of type **2** (*Scheme 2*).



1: X = Cl, Br, I, OTf
Z = $CH_2(CH_2)_2$, NHR, O

2

Scheme 2

This type of cyclization has been applied for the synthesis of large polyaromatic scaffolds, as an alternative to earlier employed harsh thermal rearrangement methodologies such as flash vacuum pyrolysis (FVP).[80,81] Shortly after the serendipitous discovery of C_{60} by Kroto *et al.*,[82] FVP was applied for the synthesis of a wide family of new bowl-shaped and related polyaromatic compounds starting from planar or almost planar polycyclic systems. One of the most remarkable examples is the seminal work by the groups of Scott and de Meijere who applied this methodology for the rational chemical synthesis of C_{60} fullerene.[83] In the presence of $TiCl_4$, trimerization of ketone **3**, which was prepared from 1-bromo-4-chlorobenzene in eleven steps, afforded trichloro derivative **4**. Pyrolysis of **4** at 1100 ºC delivered traces of C_{60} (*Scheme 3*). The amount of fullerene was estimated from the size of the C_{60} peak in the HPLC analysis and the material balance, which led to an estimated yield in the range of 0.1 to 1.0%.

80 Brown, R. F. C. *Pyrolytic Methods in Organic Chemistry: Application of Flow and Flash Vacuum Pyrolytic Techniques*; Academic Press: New York, **1980**.

81 Brown, R. F. C. *Pure Appl. Chem.* **1990**, *62*, 1981-1986.

82 Kroto, H. W.; Heath, J. R.; O'Brien, S. C.; Curl, R. F.; Smalley, R. E. *Nature* **1985**, *318*, 162-163.

83 Scott, L. T.; Boorum, M. M.; McMahon, B. J.; Hagen, S.; Mack, J.; Blank, J.; Wegner, H.;

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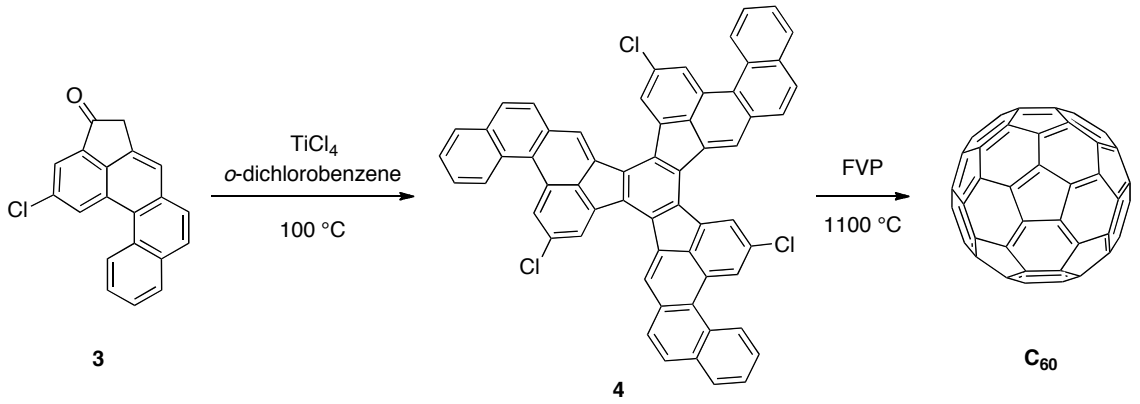

Scheme 3

Noteworthy, as showed in this example, FVP usually occurs with poor to moderate yields. Furthermore, this methodology presents other drawbacks such as low functionality tolerance and limitation to small-scale runs.[80,81] In the last decade, intramolecular direct arylation using transition metal catalysts is offering an attractive alternative for the rational design and synthesis of new PAHs in an enhanced effective manner.

Intramolecular arylations in polyaromatic systems have been often employed for the formation of several carbon-carbon bonds in a single step. In general, the synthesis of PAHs by metal-catalyzed direct arylation are carried out using palladium complexes as catalysts, in polar aprotic solvents like DMA or DMF and in the presence of base. However, metal-catalyzed arylations applied towards the synthesis of polyaromatic hydrocarbons, due to the low regioselectivity of the reaction and poor solubility of the polyaromatic final compounds, usually requires relatively high temperatures (over 100 ºC), extended reaction times (24-72 h), and the isolated yields are not always satisfactory.

Some of the more important contributions in this field have been made by Scott and co-workers that reported the Pd-catalyzed direct arylation reaction of 7,10-di(2-bromophenyl)fluoroanthene (**5**) for the synthesis of dibenzo[*a*,*g*]corannulene $C_{28}H_{14}$ (**6**) (*Scheme 4*).[84] After optimization of the reaction conditions, the desired polyaromatic product was obtained in relatively good yields (51-57%) by using

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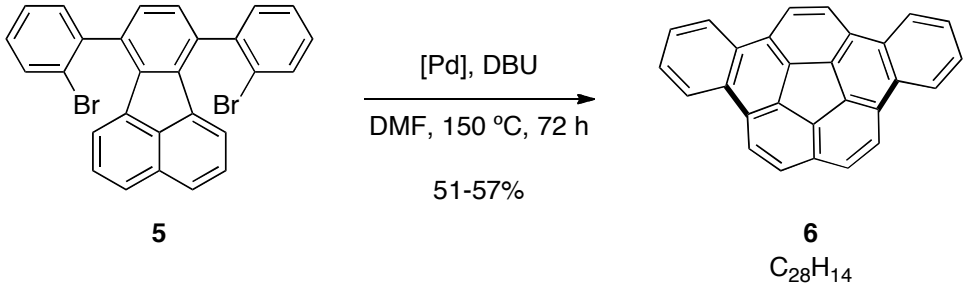
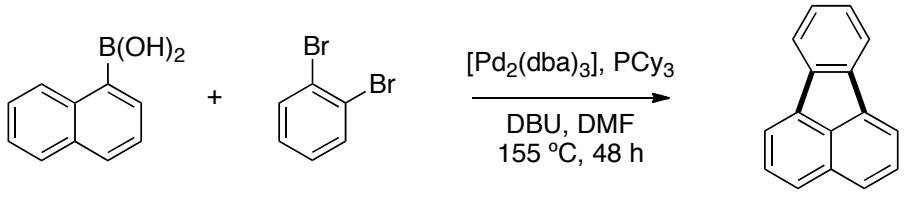
$[Pd(PPh_3)_2Br_2]$ or Hermann's palladacyle (*trans*-di(μ-acetato)-bis[*o*-(di-*o*-tolylphosphino)benzyl]dipalladium),[85] in the presence of DBU as base at 150 ºC in DMF (*Scheme 4*). This transformation had been previously achieved in a lower 38% yield from the same starting material by using FVP at 1000 ºC.[84]



5 **6** $C_{28}H_{14}$

Scheme 4

Furthermore, the groups of Scott and de Meijere developed an annulation process based on a Suzuki cross-coupling followed by intramolecular direct arylation cascade sequence. Thus, in the annulation process starting from 1-naphthylboronic acid (**7**) and 1,2-dibromobenzene, fluoroanthene $C_{16}H_{10}$ (**8**) (*Scheme 5*) was obtained in 87% yield. The best results were obtained using $[Pd_2(dba)_3]$ and PCy_3 precatalytic system, while other palladium sources like $Pd(OAc)_2$, $[PdCl_2(PPh_3)_2]$, or $[PdCl_2(MeCN)_2]$ and ligands such as PPh_3, P(*p*-tol)$_3$, P(*n*-Bu)$_3$, or dppe led to less satisfactory results.[86]



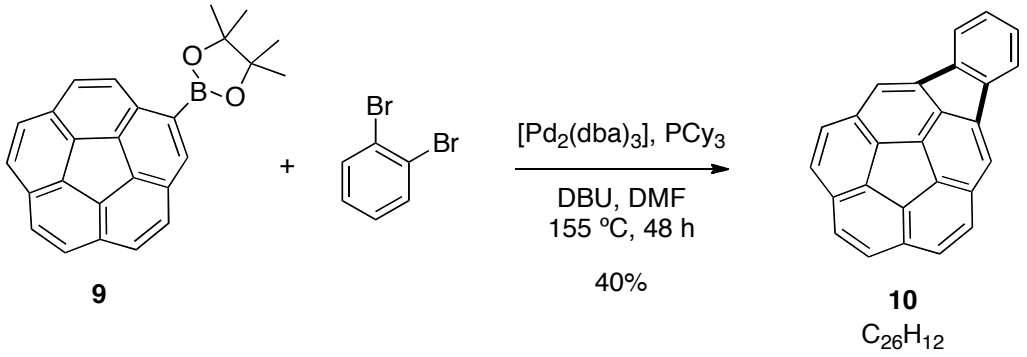
7 **8** $C_{16}H_{10}$

Scheme 5

The optimized reaction conditions were applied in the synthesis of indenocorannulene **10** from pinacol corannuleneboronate **9** and 1,2-dibromobenzene

85 Hermann, W. A.; Brossner, C.; Öfele, K.; Reisenger, C.-P.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem. Int. Ed*. **1995**, *34*, 1844-1847.

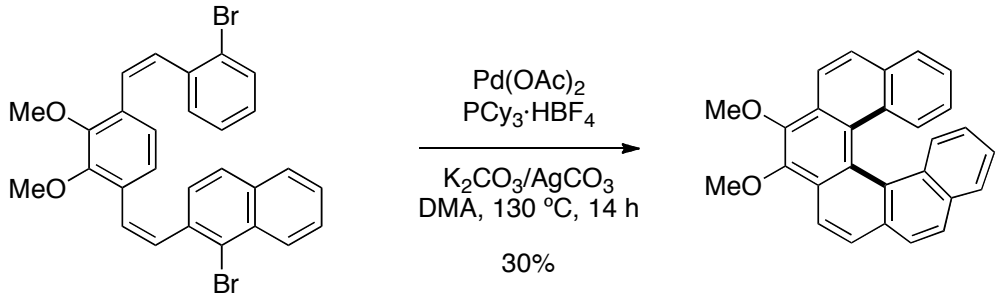
as shown in *Scheme 6*.[86]



9 **10** $C_{26}H_{12}$

Scheme 6

Kamikawa *et al*. showed that palladium-catalyzed arylation reaction might also serve as an alternative approach for the synthesis of polyaromatic helicenes. For instance, under their optimized conditions using $Pd(OAc)_2/PCy_3{\cdot}HBF_4$ as the catalytic system and $AgCO_3$ as an additive, in the presence of base K_2CO_3, a double C-H arylation of *Z,Z*-bis(stilbene) derivative **11** furnished [6]-helicene **12** in 30% yield (*Scheme 7*).[87]



11 **12**

Scheme 7

Direct arylation on triflate substrates have also been applied for the synthesis of bowl-shaped PAHs.[88] Scott and co-workers described the first synthesis of diindenopyrenes **14** and **15**, together with triindenopyrene **16** and tetraindenopyrene

87 Kamikawa, K.; Takemoto, S.; Matsuzaka, H. *J. Org. Chem*. **2007**, *72*, 7460-7408.

88 For earlier work on the arylation of aryl triflates: (a) Rice J. E.; Cai, Z. W. *Tetrahedron Lett.* **1992**, *33*, 1675-1678. (b) Rice J. E.; Cai, Z. W. *J. Org. Chem.* **1993**, *58*, 1415-1424. (c) Rice

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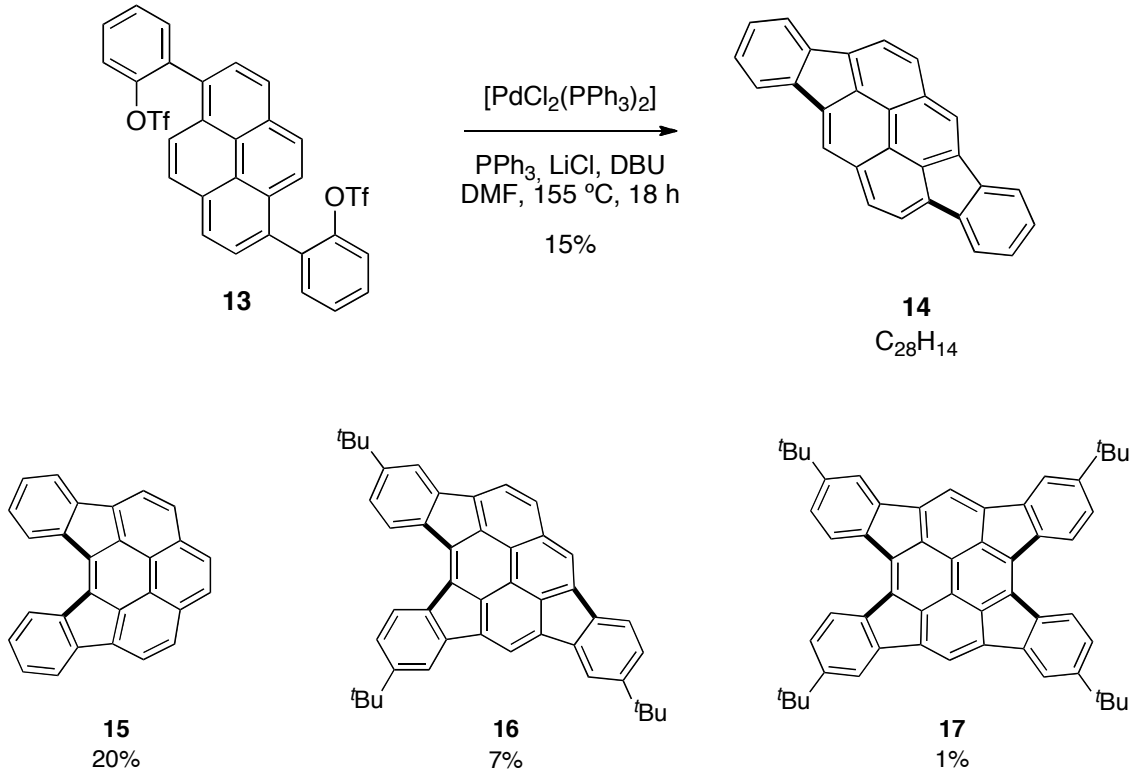
17,[89] using conditions previously developed in their group (*Scheme 8*).[84] These PAHs were obtained, although in low yields, from the intramolecular palladium catalyzed direct arylation of the corresponding triflate substituted pyrenes like **13**.



Scheme 8

Better yields of **14** and its regioisomer **15** were obtained starting from the corresponding dibromide substrates.[89] Compounds **14** to **17** were reported to be stable and to have intense red colors. These physical properties makes them promising candidates for their applications as long wavelength dyes when high temperature conditions are required.[89]

The group of Shevlin early found a system based on $[PdCl_2(PCy_3)_2]$/DBU for the synthesis of bowl-shaped fullerene fragments using aryl chlorides as substrates.[90] The same polyarenes could be synthesized with $[PdCl_2(PPh_3)_2]$/DBU or NaOAc starting with the aryl bromide or triflate in very good yields.[90]

89 Wegner, H. A.; Reisch, H.; Rauch, K.; Demeter, A.; Zachariasse, K. A.; de Meijere A.; Scott, L. T. *J. Org. Chem.* **2006**, *71*, 9080-9087.

90 (*a*) Wang L.; Shevlin, P. B. *Tetrahedron Lett.* **2000**, *41*, 285-288. (*b*) Wang L.; Shevlin, P.

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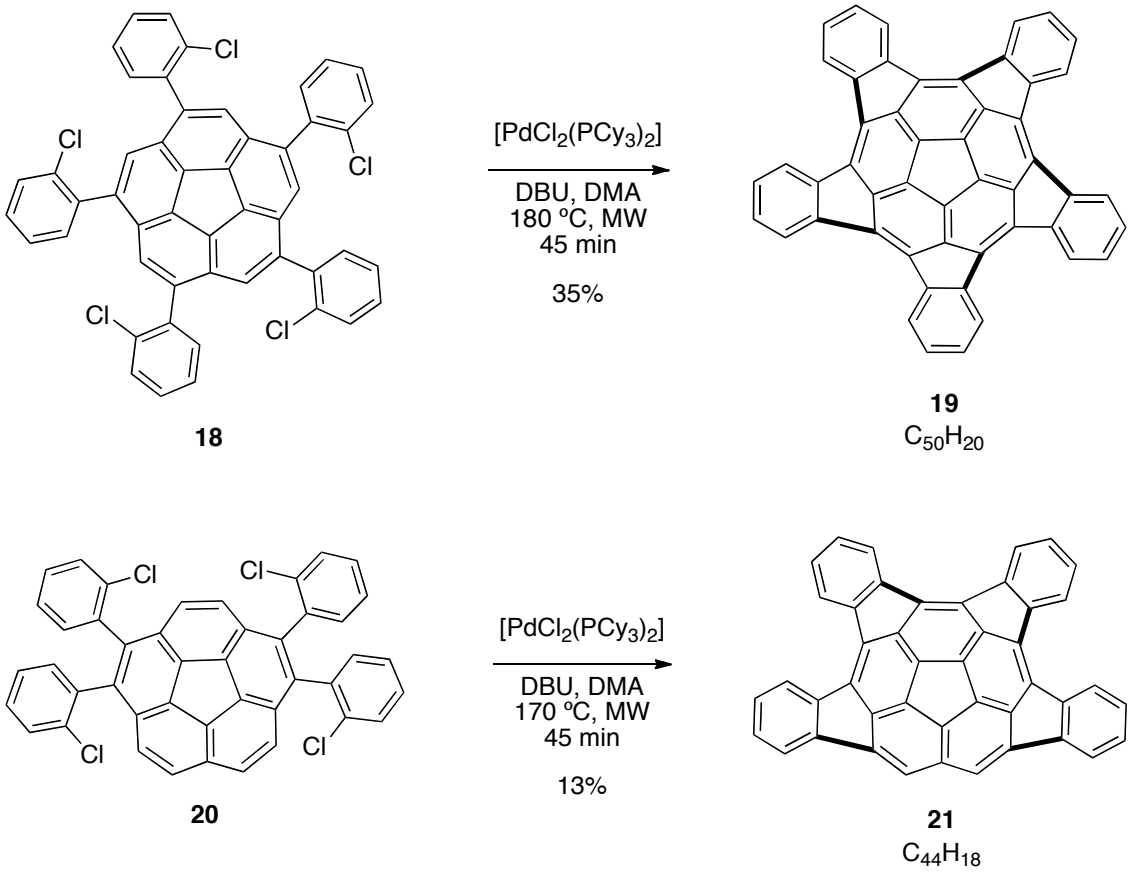
Later, using a similar catalytic system, Scott *et al*. succeeded in the synthesis of two new geodesic polyarenes: pentaindenocorannulene **19** ($C_{50}H_{20}$) and tetraindenocorannulene **21** ($C_{44}H_{18}$) (*Scheme 9*), the largest curved subunits of C_{60} prepared until then.[91] Derivative **19** was obtained in 35% isolated yield (81% average yield per C-C bond formation) from 1,3,5,7,9-pentakis(2-chlorophenyl)corannulene (**18)** through a palladium catalyzed and microwave induced (180 ºC, 45 min) five-fold intramolecular arylation reaction. Tetraindenocorannulene **21** was prepared from 1,2,5,6-tetrakis(2-chlorophenyl) corannulene (**20**) under similar conditions although only in 13% isolated yield. Competitive couplings between neighboring chlorophenyl rings could explain the lower yield in the synthesis of **21**.



Scheme 9

91 Jackson, E. A.; Steinberg, B. D.; Bancu, M.; Wakamiya, A.; Scott, L. T. *J. Am. Chem. Soc.*

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As the authors pointed out,[91] these achievements demonstrate that rational chemical synthesis of fullerenes, carbon nanotubes and related carbon rich molecules should be possible using solution chemical methods avoiding the employment of less efficient gas-phase pyrolysis methodologies like FVP. In this regard, the application of direct arylation using similar microwave conditions has given access to the whole family of indenocorannulenes, including all the seven members of the family: indenocorannulene, both isomers of diindenocorannulene, both isomers of triindenocorannulene, tetraindenocorannulene and pentaindenocorannulene. These range in size from $C_{26}H_{12}$ to $C_{50}H_{20}$ and all map onto the bowl-shaped framework of C_{60}.[92]

Palladium-catalyzed direct arylation has also been applied in our research group for the synthesis of fullerene fragments. Our synthetic approach is based on the intramolecular arylation of functionalized bromoaryl truxenes, readily available by triple alkylation of truxene.[93] Thus, cyclization of syn or anti truxene **22** has been performed under phosphorus free conditions introduced by Jeffery,[94] using $Pd(OAc)_2$ as precatalyst, $BnMe_3NBr$ quaternary ammonium salt, carbonate base in DMF or DMA at high temperatures (130-150 ºC). Under these conditions, tribromobenzyltruxene **22** delivered the non-planar polyarene $C_{48}H_{24}$ **23** in good isolated yields (71 to 79%) with an average of 89 to 92% yield for each C-C bond formed (*Scheme 10*).[9] In addition to the triple cyclization, under the reaction conditions the arylated compound suffers dehydrogenation to form the fully aromatic compound.

92 Steinberg, B. D.; Jackson, E. A.; Filatov, A. S.; Wakayami, A.; Petrukhina, M. A.; Scott, L. T. *J. Am. Chem. Soc.* **2009**, *131*, 10537-10545.

93 (a) de Frutos, Ó.; Gómez-Lor, B.; Granier, T.; Monge, M. Á.; Gutiérrez-Puebla, E.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **1999**, *38*, 204-207. (b) Gómez-Lor, B.; de Frutos, Ó.; Ceballos, P. A.; Granier, T.; Echavarren, A. M. *Eur. J. Org. Chem.* **2001**, 2107-2114. (c) Gómez-Lor, B.; González-Cantalapiedra, E.; Ruiz, M.; de Frutos, Ó.; Cárdenas, D. J.; Santos, A.; Echavarren, A. M. *Chem. Eur. J.* **2004**, *10*, 2601-2608.

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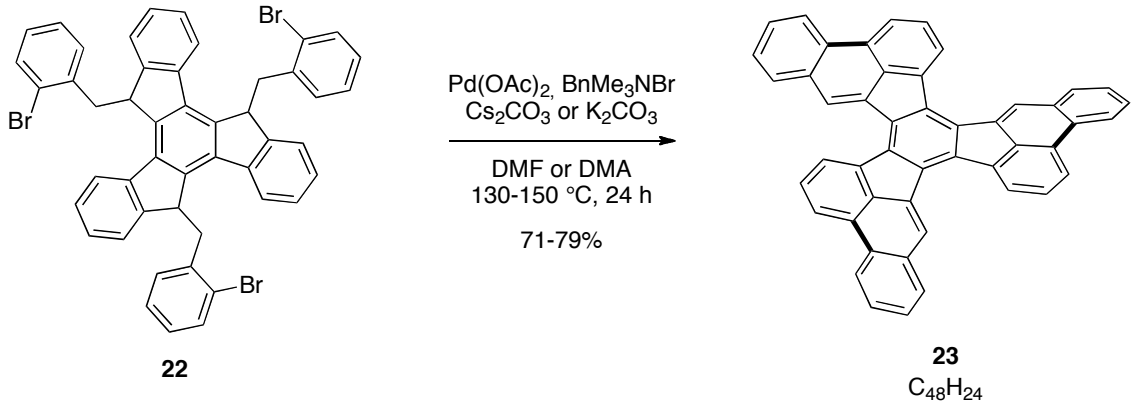
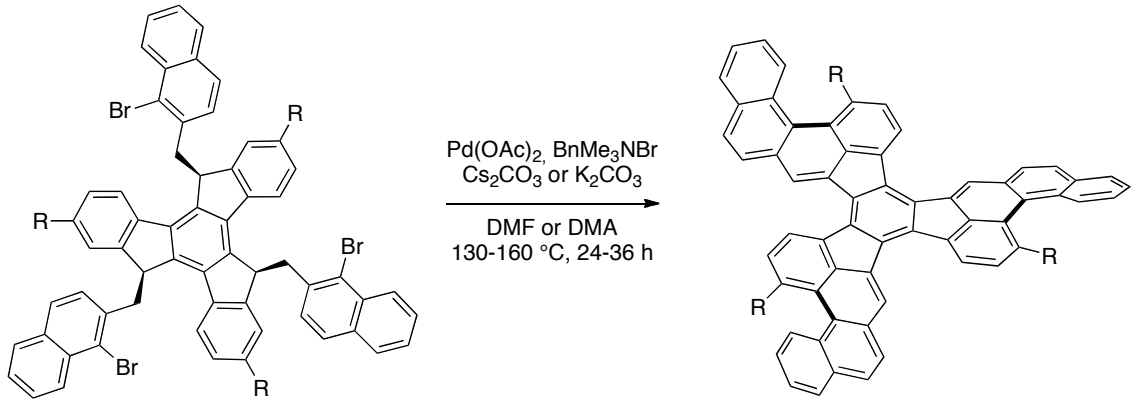


22 **23** $C_{48}H_{24}$

Scheme 10

Similarly, intramolecular arylation of naphthyl derivatives **24a-c** furnished the polyaromatic hydrocarbons **25a-c** although in moderate yields (26-53%) (*Scheme 11*).[9,95]



24a-c

25a: R = H, 53%
25b: R = Bu, 26%
25c: R = Ph, 38%

Scheme 11

The triaza-analogue **27**, could also be prepared via direct arylation of *N*-alkylated triindoles such as **26** under slightly milder conditions in a satisfactory yield (64%, meaning an average of 86% yield for each C-C bond forming process) (*Scheme 12*).[96]

95 (a) Gómez-Lor, B.; de Frutos, Ó.; Echavarren A. M. *Chem. Commun.* **1999**, 2431-2432. (b) Gómez-Lor, B.; Koper, C.; Fokkens, R. H.; Vlietstra, E. J.; Cleij, T. J.; Jenneskens, J. L.; Nibbering, N. M. M.; Echavarren, A. M. *Chem. Commun.* **2002**, 370-371.

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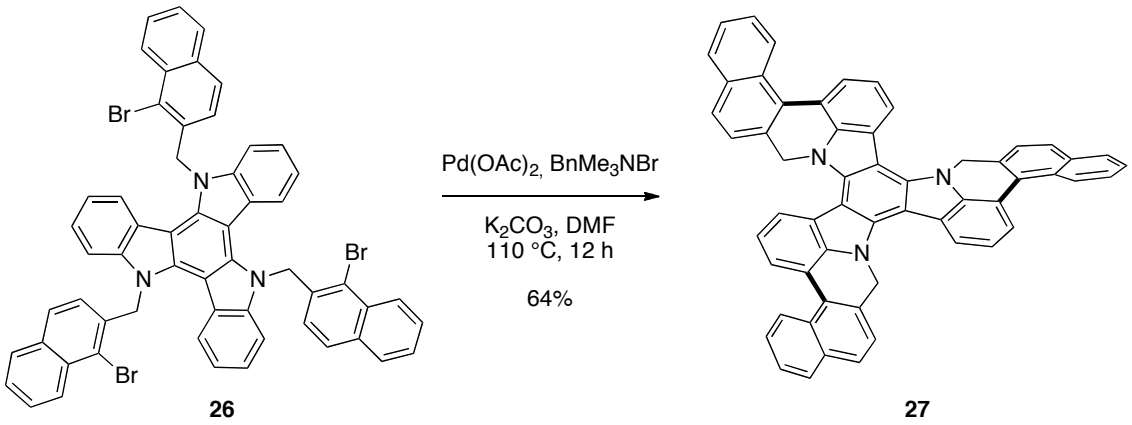
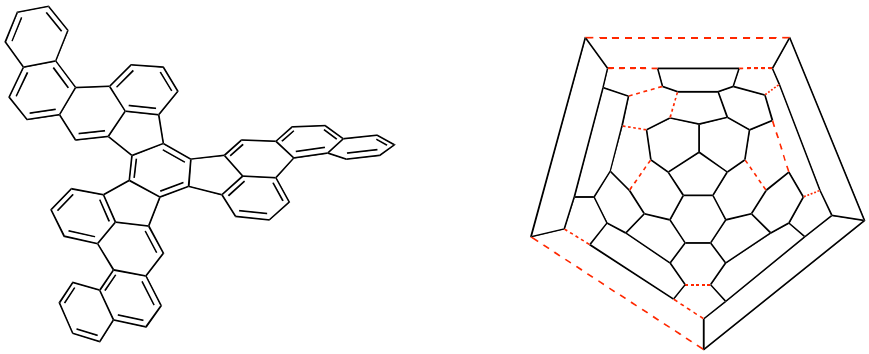


Scheme 12

A key feature of **25a**, $C_{60}H_{30}$, based on a decacyclene core fused with three naphthyl units, is the incorporation of the exact carbon atom topology of the C_{60} as shown in Schlegel diagram (*Figure 8*). Polyarene **25a** can bee seen as a crushed C_{60} fullerene as it corresponds to a hypothetical hydrogenolysis product of C_{60}. Remarkably, by using mass spectrometric techniques, at high laser fluences, $C_{60}H_{30}$ was converted into $C_{60}^{\cdot+}$ via a fifteen-fold stepwise consecutive intramolecular cyclodehydrogenations processes.[95b] This renders **25a** as a synthon for endohedral C_{60} formation and suggests that fullerene C_{60} is build up from $C_{60}H_{30}$ by molecular transformation and not by fragmentation and recombination in the gas phase.[97] Independent work carried out at the same time in the group of Scott, showed the same transformation of **25a** to $C_{60}^{\cdot+}$ using LDI-MS.[98]



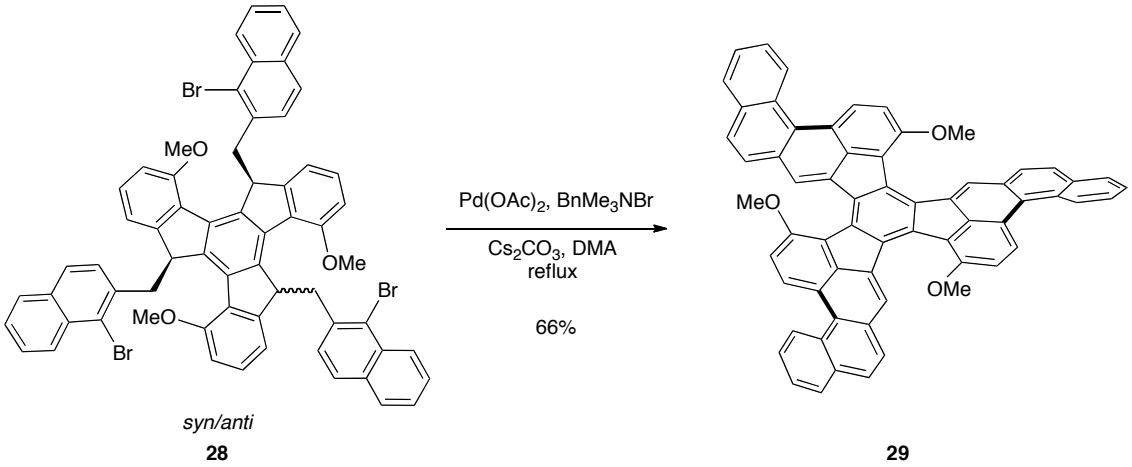
25a
$C_{60}H_{30}$

Schlegel diagram
$C_{60}H_{30}$

Figure 8: $C_{60}H_{30}$ Molecular structure and Schlegel representation.

97 Nierengarten, J.-F. *Angew. Chem. Int. Ed.* **2001**, *40*, 2973-2974 and references therein.

Another step forward towards the rational synthesis of C_{60} that has been developed in our research group, is the cyclization of bromonaphthyl derivative **28** to form $C_{63}H_{27}O_3$ **29**, bearing three methoxy substituents at C-3, C-13 and C-23 strategic positions of the truxene core (*Scheme 13*).[9b]



Scheme 13

The methoxy groups were transformed to the corresponding triflates via a two-step demethylation/triflation process. After several attempts for triple arylation of the triflate derivative **30**, microwave promoted reaction (200 W, 10 min) in the presence of $[PdCl_2(PPh_3)_2]$, LiCl and DBU in DMA led to a mixture of products that was analyzed by mass spectrometry (*Scheme 14*). MALDI-MS experiments showed, among others, a peak at *m/z* 721 that can be attributed to $(C_{60}+H)^+$ and a peak at *m/z* 851 that can be assigned to the triarylated compound **31** $(C_{60}H_{24}+Ag)^+$.[99]

99 Esther González Cantalapiedra, *Doctoral Thesis*, Universidad Autónoma de Madrid,

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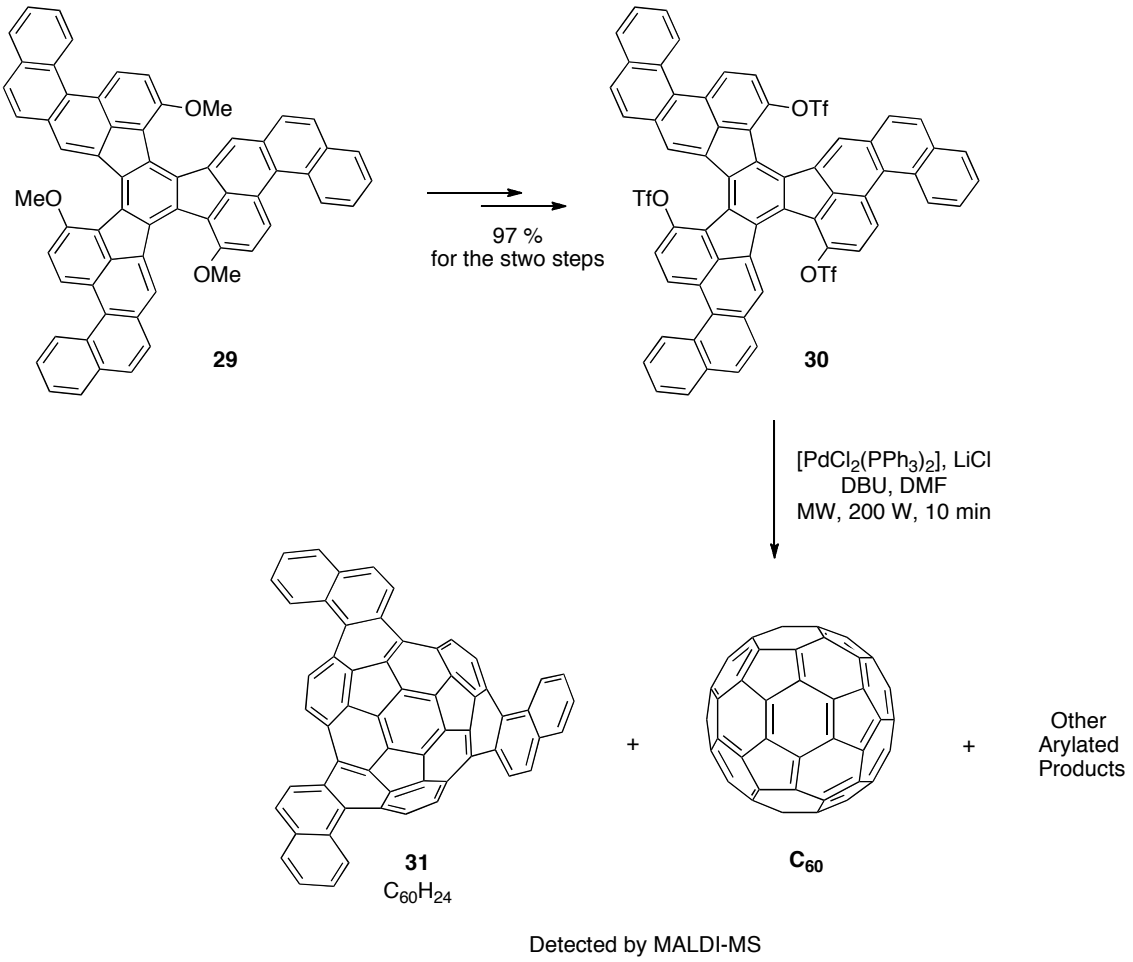

Scheme 14

The amount of C_{60} produced in the final step was qualitatively analyzed by HPLC and an estimated yield of 0.23% was determined, which is comparable with that reported by Scott.[83]

Using the same palladium-catalytic system, a triple cyclization has also been performed on hexamethoxy substituted truxene **32** to give **33** in 40% yield that, after demethylation/triflation, could undergo an unprecedented hexaarylation reaction to give $C_{60}H_{18}$ in one single step.[99,100] However, all the attempts for the transformation of OMe into triflate groups have been unsuccessful until now (*Scheme 15*).

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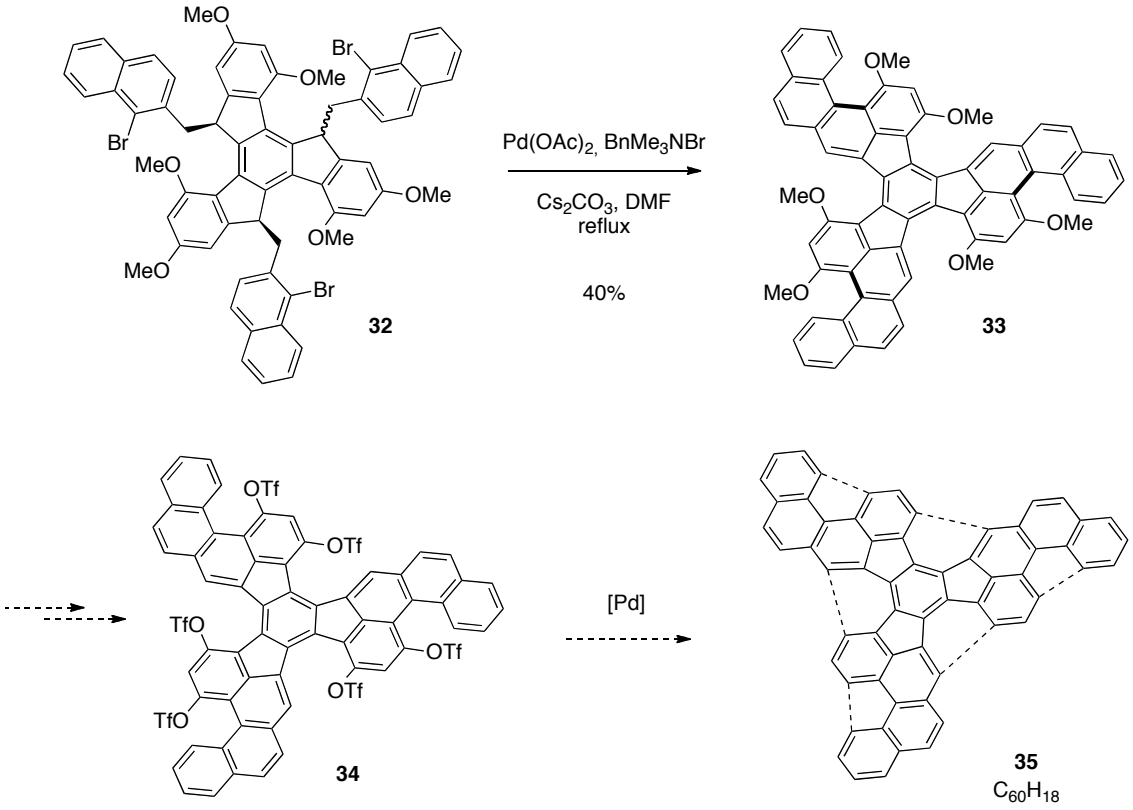

Scheme 15

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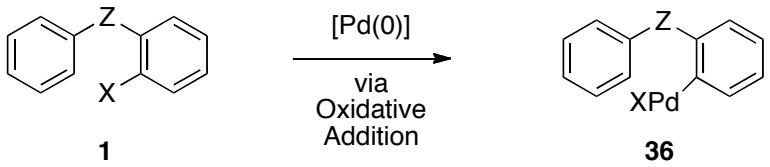
1.2 Mechanistic Aspects of Pd-Catalyzed Intramolecular Direct Arylation[101]

Despite the significant progress that has been made on the application of the intramolecular direct arylation for the formation of five and six member rings in the synthesis of PAHs and related systems, less attention has been paid on the insights of the possible mechanisms that proceed in this transformation. Understanding the mechanism is crucial in terms of rational design and for the development of novel synthetic procedures for the preparation of new potential candidates in molecular materials.

As it was pointed out before, intramolecular direct arylation takes place on substrates of general type **1**, where X = Cl, Br, I or OTf, to form carbo- and heterocycles **2**.[71] It is generally accepted that in the first step, an oxidative addition of **1** to [Pd(0)] leads to [Pd(II)] complexes [$ArPdXL_2$] **36** (*Scheme 16*).



1 **36**

Scheme 16

Further on, several mechanisms have been proposed for the subsequent pathways that, through C-H bond activation, evolve to the arylated compounds **2**. Different authors have proposed: (a) an electrophilic aromatic substitution (S_EAr) via intermediate **37**, (b) a σ-bond metathesis through intermediate **38** and (c) a Heck-type process via **39** (*Scheme 17*).

101 Recently, we have contributed with a chapter that summarizes all the mechanistic studies on the arylation reactions that have been carried out in certain detail: De Mendoza, P.; Echavarren, A. M. In *Mechanistic Aspects of Transition Metal-Catalyzed Direct Arylation Reactions;* Ackermann, L., Ed.; Wiley-VCH: Weinhein, **2009**, Chapter 11, pp 363-499. In the present manuscript, we focus on the intramolecular version of the palladium catalyzed direct arylation of aromatic compounds, excluding the arylation of heteroaromatic substrates or the reaction via metallacycles assisted by functional groups that promote *ortho*-

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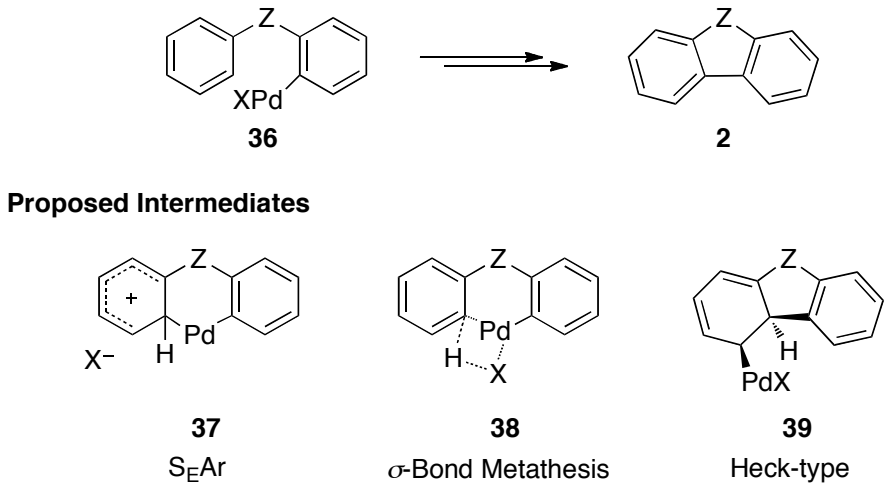

Scheme 17

Although the precise mechanism of a particular reaction may depend on the nature of the substrate, catalyst, ligand, and solvent employed, most authors have favored an electrophilic aromatic substitution considering that the initially formed [$ArPdXL_2$] complex would react as metal electrophile with the arene ring **37**.[102,103] An interesting mechanistic alternative is a σ-bond metathesis via intermediates **38**,[104,105] which, according to computational studies,[105] seems more likely than processes involving C-H oxidative addition via a [Pd(II)]/[Pd(IV)] catalytic cycle.[106,107] An insertion into the arene to form **39** by a Heck-type process has also been proposed.[108] However, later work using an enantiopure substrate indicates that this process is rather unlikely.[109]

---

102 (a) Catellani, M.; Chiusoli, G. P. *J. Organomet. Chem.* **1992**, *425*, 151-154. (b) Martín-Matute, B.; Mateo, C.; Cárdenas, D. J.; Echavarren, A. M. *Chem. Eur. J.* **2001**, *7*, 2341-2348.

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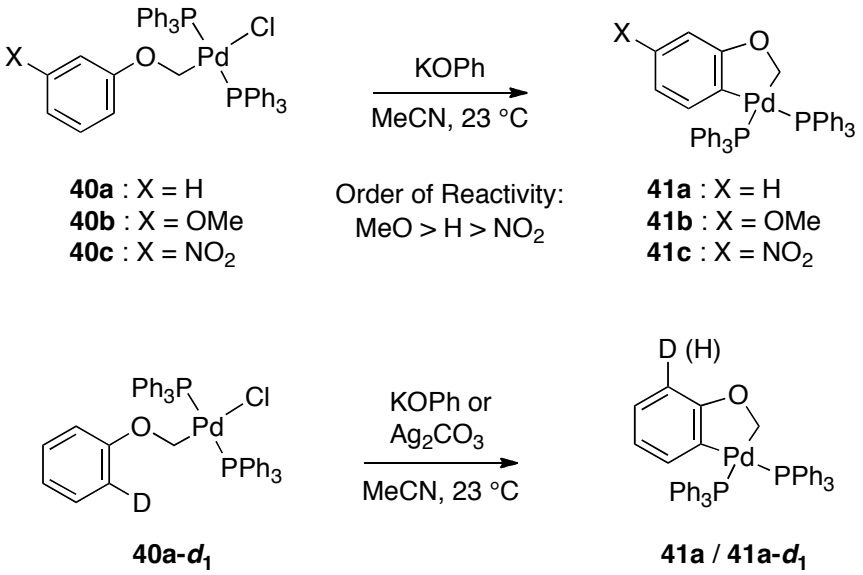
In order to determine the mechanism, substituent effects on the intramolecular palladation were studied in our research group starting with alkyl palladium complexes **40a-c** and KOPh as base to form five-membered palladacycles **41a-c** (*Scheme 18*).[102b] This reaction was shown to follow the order of reactivity MeO > H > NO_2 for sustituents para to the reacting site as expected for an electrophilic aromatic substitution mechanism. Nonetheless, the arylation reaction tolerates both electron-releasing and electron-withdrawing groups, which casts doubts on the S_EAr mechanism proposed.[110] The activation of monodeuterated substrate **40a-*d*$_1$** with KOPh or Ag_2CO_3 in MeCN at 23 ºC led to the palladacycles **41a**, partially deuterated at C-3. The deuteration degree determined by ^{1}H NMR (48±3%), shows that, as it has been observed for most electrophilic aromatic substitutions,[111] there is no isotopic effect for the intramolecular C-H activation by the alkylpalladium. This result demonstrates that the C-H bond breaking event does not take place during the rate determining step.[102b] The same order of reactivity had earlier been found on the palladation of related substrates bearing the same substituents.[102a]



Scheme 18

110 González, J. J.; García, N.; Gómez-Lor, B.; Echavarren, A. M. *J. Org. Chem.* **1997**, *62*, 1286-1291.

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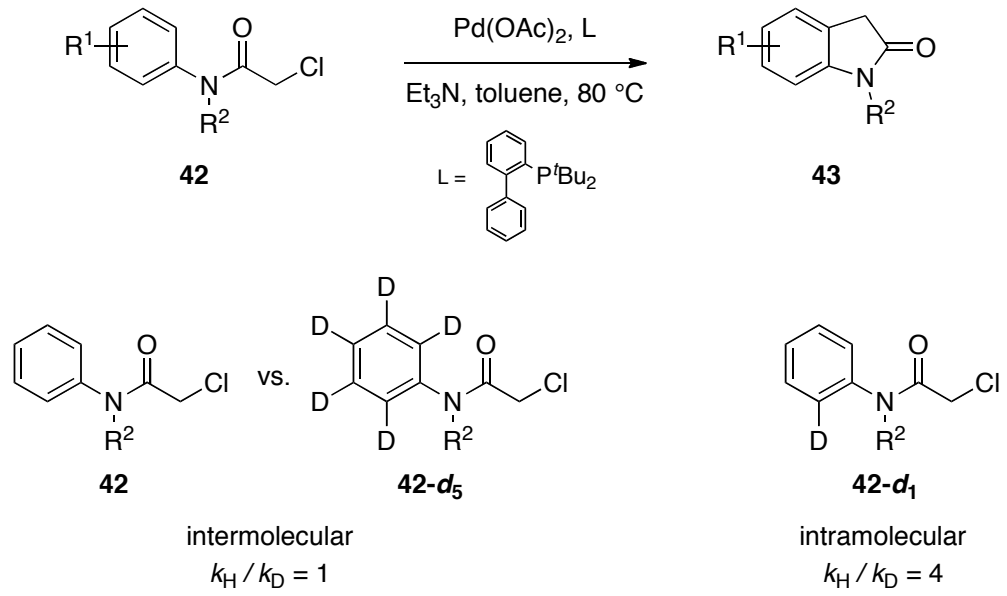
Although, according to the order of reactivity, these experiments may suggest that the palladation proceeds by an electrophilic aromatic substitution, inconsistent results like the tolerance of nitro-substituents on the direct arylation, shows that these transformations are probably more complex. Indeed, reaction of alkyl palladium complex **40a** was almost completely inhibited by addition of 1 equiv of PPh_3, indicating that ligand substitution may occur during the C-H activation process, while slower reactivity was observed when using bidentate phosphine ligands.[102b]

The group of Buchwald also studied the isotopic effects in the palladiumd-catalyzed cyclization of substrates **42** to form oxindoles **43** via C-H functionalization (*Scheme 19*).[112] Whereas no kinetic isotope effect was observed in the competitive reaction of **42** and **42-*d*$_5$**, an intramolecular primary isotope effect of $k_H/k_D = 4$ was found in the cyclization of the *ortho*-monodeuterated substrate **42-*d*$_1$**. The absence of an intermolecular isotope effect suggests that the first step, the oxidative addition, is slow and rate determining overall. On the other hand, the significant intramolecular isotope effect shows that, in this case, the palladation is reversible and fast relative to the C-H bond cleavage step, or that a true C-H activation is involved in this reaction.



Scheme 19

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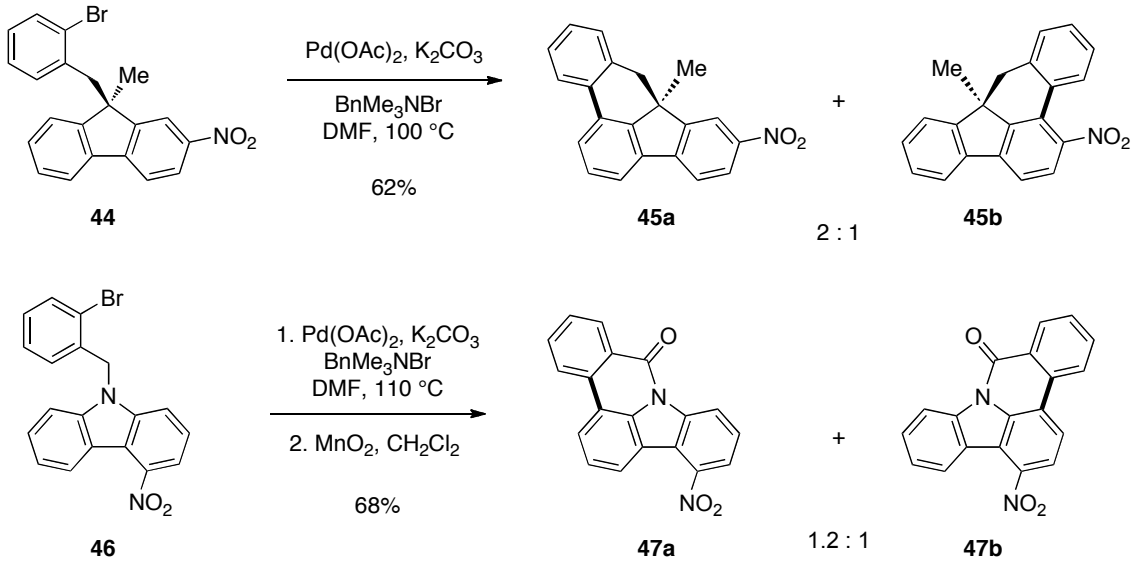
Substituted fluorenes[110] and carbazoles[96] have also been employed in our group for studying the substituent effects in the direct arylation process with electron-withdrawing groups. Thus, the reaction of nitrofluorene **44** afforded a 2:1 mixture of regioisomers **45a** and **45b**, favoring formation of the C-C bond on the non-substituted aromatic ring (*Scheme 20*). However, this slight preference for the formation of **45a**, not significant in energetic barrier terms, could also be explained by the steric effect exerted by the nitro group. Under similar conditions, nitrocarbazole **46**, a less sterically biased substrate, gave an almost equimolar mixture of arylated products. To facilitate the determination of the regiosisomeric ratio, the arylated compounds were oxidized with MnO_2 yielding a 1.2:1 mixture of lactams **47a** and **47b** (*Scheme 20*). The formation of significant amounts of arylation products ortho or para to a strongly electron-withdrawing nitro group again is not consistent with an electrophilic aromatic substitution mechanism.



Scheme 20

To study the regioselectivity of the reaction, Fagnou and co-workers probed the arylation using differently substituted ethers **48**. In general, arylations occurred with good selectivities at the less hindered para position favoring the formation of isomer **49a** (*Scheme 21*).[113] Of particular interest is the arylation of the compound with a fluorine substituent, which led to an inversion on the regioselectivity giving isomer

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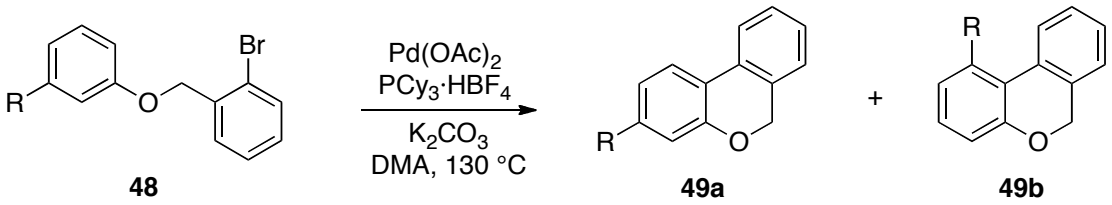
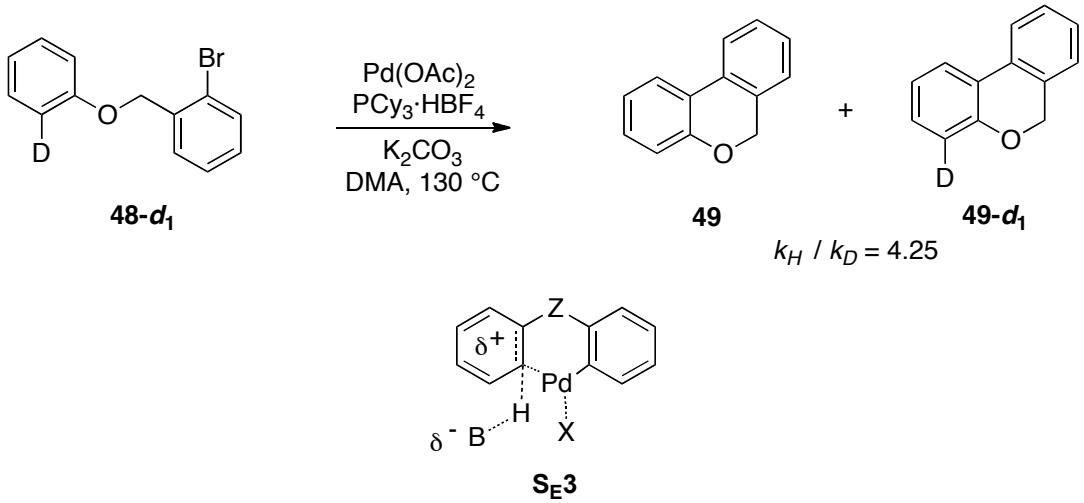
49b as the major compound. This result, where lower steric effects can be considered, indicates that the electron-withdrawing fluorine atom exerts an inductive influence that favors the reaction at the ortho rather than the para position.



R = OMe, Me, *i*-Pr, *t*-Bu, CF_3, NO_2, CO_2Me: ratio **49a**/**49b** = 10:1 to > 30:1
R = Cl: ratio **49a**/**49b** = 3.2:1
R = F: ratio **49a**/**49b** = 1:4.3

Scheme 21

Moreover, the direct arylation of the partially deuterated compound **48-*d*$_1$** resulted in a primary kinetic isotopic effect of 4.25 *(Scheme 22)*.[113] This study revealed the significant influence of the C-H bond cleavage step on the reaction rate during the arylation. The authors rationalized this result with a mechanism proceeding via electrophilic metallation involving either a σ-bond metathesis or a C-H functionalization step via a concerted palladation-deprotonation process following a formal S_E3 mechanism,[111] as shown in *Scheme 22*.[113]



Scheme 22

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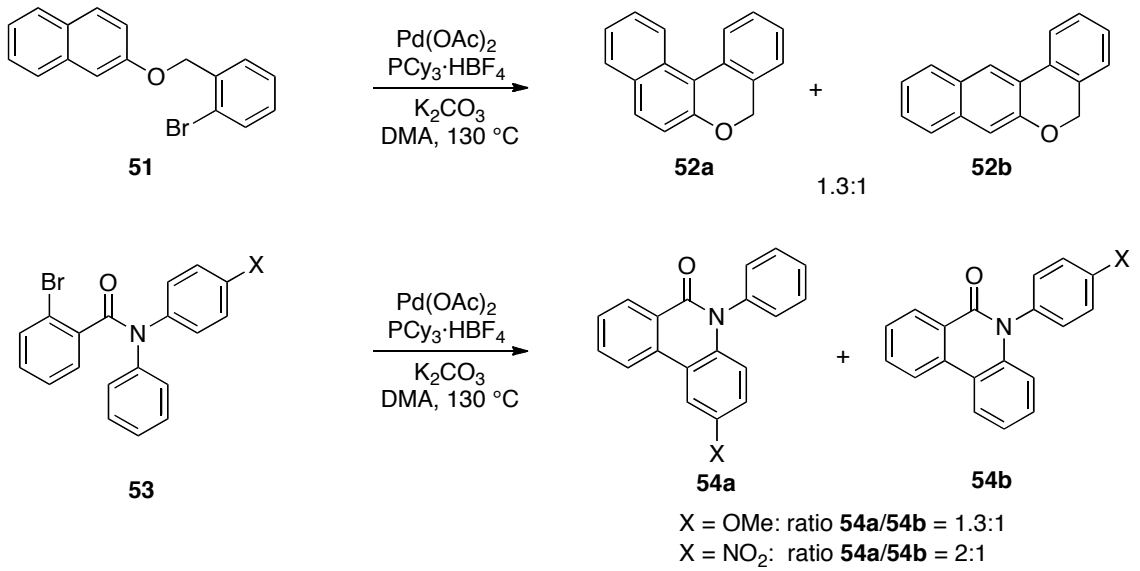
Low regioselectivities were also observed in the reaction of substrates **51** and **53** (*Scheme 23*).[113] However, the interpretation of the results with substrate **53** might be complicated by the competing amide rotation, which may lead to a system far from Curtin-Hammett conditions.



Scheme 23

Recently, in our research group, substrates **55a-d** with an alkyl tether CH(R) between two differently substituted aryls were prepared. These compounds present minimum steric and/or electronic bias, and therefore, a more precise study of the effect of the substituents in the intramolecular arylation could be preformed (*Scheme 24*).[114]

114 García-Cuadrado, D.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem. Soc.*

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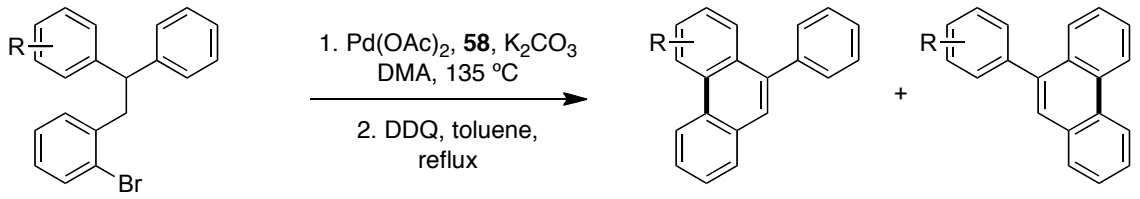
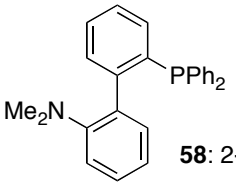


55a: R = 4-OMe
55b: R = 4-CF_3
55c: R = 4-Cl
55d: R = 3,4,5-$(F)_3$

56a/57a = 1.1:1 (90%)
56b/57b = 1.3:1 (71%)
56c/57c = 1.5:1 (66%)
56d/57d = **25:1** (82%)



58: 2-(Diphenylphosphino)-2'-(*N,N*-dimethylamino)biphenyl

Scheme 24

In these examples, with substrates bearing electron-releasing (OMe) or electron-withdrawing (Cl, CF_3) groups in S_EAr processes, similar regioisomeric ratios (1.1-1.5:1) favoring the reaction at the substituted aryl ring were obtained under the arylation conditons. Noteworthy, in S_EAr processes, the electron lone pairs of methoxy groups stabilize the Wheland cationic intermediates lowering the activation energy and, as resonance effects overweigh inductive effects, methoxy substituents are activators in this transformation. In contrast, in the case of halogen substituents their negative inductive effect preponderates deactivating the aryl ring towards electrophilic substitutions. The fact that the methoxy group behaves similarly to the chlorine substituent in the direct arylation indicates that the mesomeric effect does not have the same influence as in the S_EAr mechanism, and that both substituents are exerting a similar inductive effect.

Remarkably, reaction of **55d**, with three electron-withdrawing fluorine substituents, occurred almost exclusively at the trifluorophenyl ring to give **56d**/**57d** in a 25:1 ratio, confirming the strong inductive effect of fluorine atoms, which again is totally inconsistent with a mechanism proceeding through an electrophilic substitution.

In addition, arylation of deuterated substrate **55e** gave an intramolecular isotope effect of $k_H/k_D = 5.0$ and 6.7 at 100 ºC in DMF and at 135 ºC in DMA, with 92% and 82%

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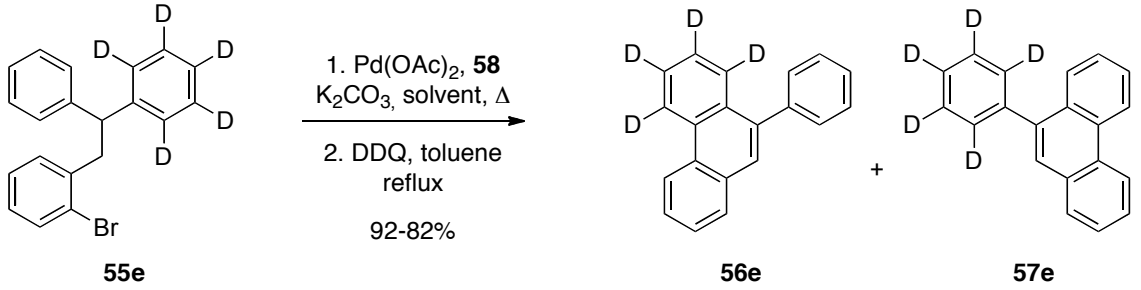
yield, respectively (*Scheme 25*), indicating that the C-H bond is cleaved in the rate determine step.

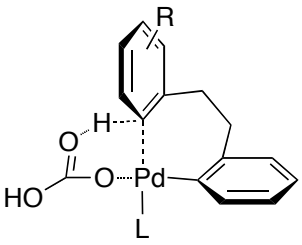


55e **56e** **57e**

Scheme 25

To support these experimental evidences in which arylation takes place on electron-deficient rings, DFT studies on the mechanism of the reaction were carried out. In agreement with experimental data, and in contrast to what would be expected in a S_EAr mechanism, theoretical results on simplified model systems (see *Figure 9*), demonstrated that the palladium-catalyzed arylation in substrate of type **55d**, with three fluorine atoms in one of the aryls, is energetically favored compared to model substrate **55** without substituents in the aryl rings.[114]

These results, where reaction is favored on C-H acidic arenes, suits better with a mechanism where the hydrogen from the phenyl is transferred as a proton in the step determining the selectivity. According to DFT studies, the most plausible pathway is through a proton abstraction mechanism assisted by a carbonate or related ligand. Transition state **I** was proposed providing a satisfactory explanation for experimental and theoretical data (*Figure 9*).



I

Figure 9: Proposed transition state on the base assisted proton abstraction mechanism.

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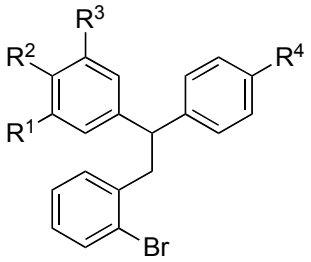
2. Objectives

The emerging developments on the palladium-catalyzed direct arylation for the synthesis of new large non-planar aromatic systems and the recent mechanistic studies where a change of paradigm has been established, led us to undertake the following challenges:

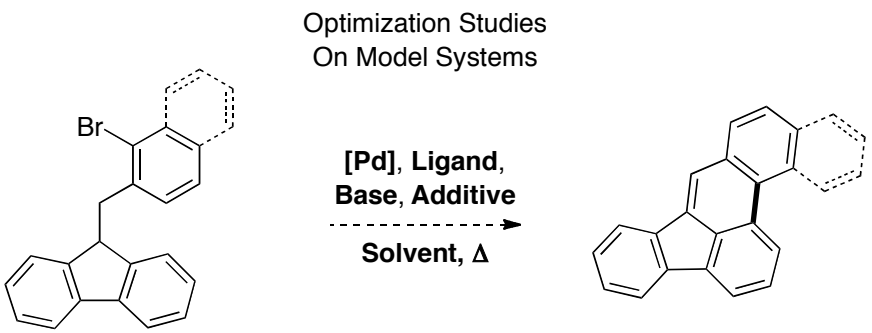
In the first place, we planned to study in detail the influence of the substituents in the proton abstraction mechanism. For this aim, we decided to investigate the regioselectivity on the intramolecular arylation with new substrates **55** bearing different electron-withdrawing and electron-donating substituents at various positions on the aryl rings (*Figure 10*).



55

Figure 10: New substrates with different substitutents for regioselective studies on the intramolecular palladium-catalyzed direct arylation.

Further on, we decided to explore the optimal reaction conditions for the intramolecular direct arylation for its application on the synthesis of novel polyaromatic systems under milder and more efficient conditions than the currently employed.



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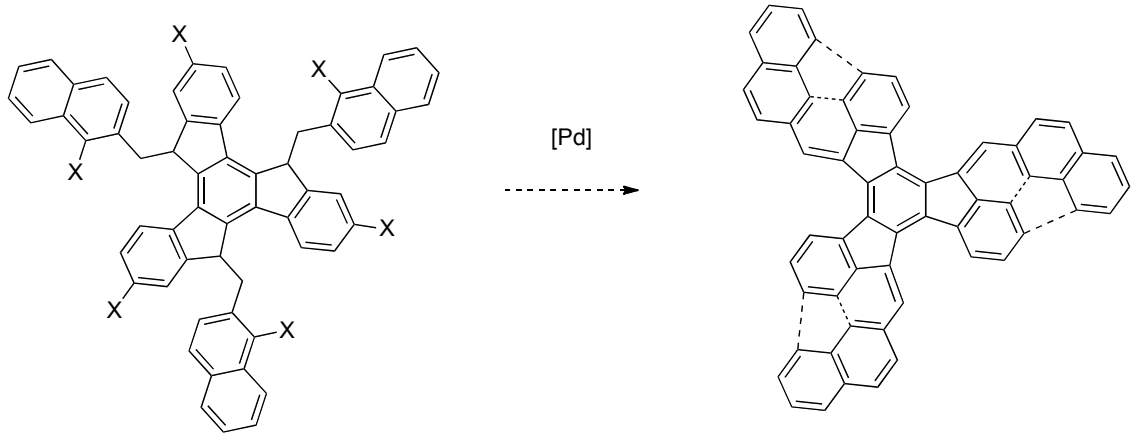
Special interest was focused on the preparation of new C_{60} crushed fullerenes like $C_{60}H_{24}$. For the synthesis of this carbon-rich crushed fullerene, we planned to prepare an hexa-functionalized truxene precursor to apply the metal-catalyzed cyclization and form six new C-C bonds in an unprecedented single step, as a new milestone towards the rational synthesis of C_{60} fullerene (*Scheme 27*).



$C_{60}H_{36}X_6$ **$C_{60}H_{24}$**

Scheme 27

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3. Results and Discussion

3.1 Mechanistic Studies

3.1.1 Substituent Effects

To investigate the base assisted proton abstraction mechanism we wanted to study the influence of the substituents in the regioselectivity of the reaction. In particular, due to the large effects that three fluorine atoms exerted on the regioisomeric ratios obtained on substrate **55d** (see *Scheme 24*), we wanted to deeply explore the effect of fluorine atoms and investigate their inductive directing effect. Therefore, we prepared substrates **55f** with a single fluorine atom at the meta position and **55g** with two fluorine atoms at the ortho position of the reacting site. An additional difluorinated substrate, **55h**, in which the arylation can take place at two different positions of the substituted ring, was also prepared (*Figure 11*).[115]

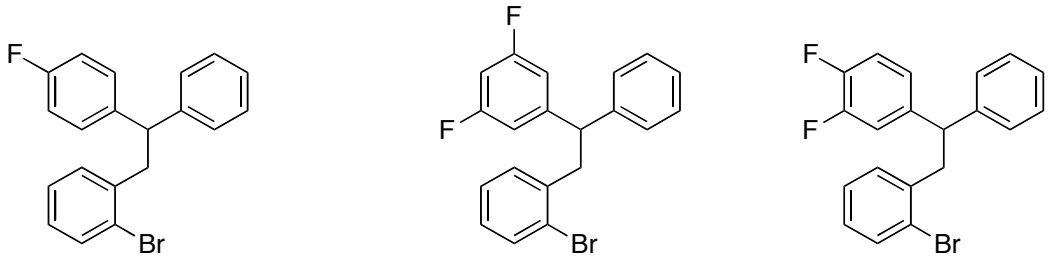

Figure 11: Different fluorine substituted substrates for the Pd-catalyzed arylation reaction.

To invert the regioselectivity, and favor the reaction to take place on the unsubstituted ring, substrates **55i** and **55j**, bearing electron-donating *t*-Bu and $SiMe_3$ groups, respectively, were also prepared (*Figure 12*). In contrast to OMe substituent, which, due to mesomeric effects can behave as electron-releasing group, *t*-Bu, and $SiMe_3$ substituents at meta position from the reacting site, avoiding possible steric influence, will allow us to consider exclusively electron-donating inductive effects.

115 García-Cuadrado, D.; de Mendoza, P.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J.*

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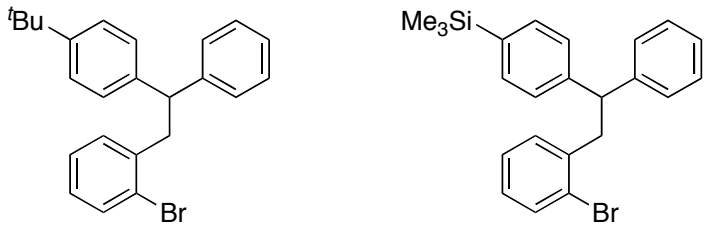
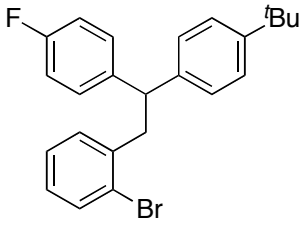


55i **55j**

Figure 12: Different electron-donating substituted substrates for the Pd-catalyzed arylation reaction.

Finally, we prepared a substrate with different electronic character substituents on each of the aryl rings. Compound **55k** with both, electron-releasing and electron-withdrawing groups, was prepared (*Figure 13*) to study if the selectivity in the palladium-catalyzed intramolecular direct arylation could be enhanced, favoring even more the reaction on the electron-deficient fluorine-containing ring.



55k

Figure 13: Substrate with an electron-donating an electron-withdrawing group in each of the aryl rings for the Pd-catalyzed arylation reaction.

The preparation of substrates **55f-k** were accomplished following the synthetic route shown in *Scheme 28* developed by Dr. Domingo García-Cuadrado.[114] The synthesis is based on the reduction of tertiary alcohol **59** derived from the addition of *ortho*-bromophenylmethylmagnesium bromide **61** to the corresponding substituted benzophenones **60** (*Scheme 28*).

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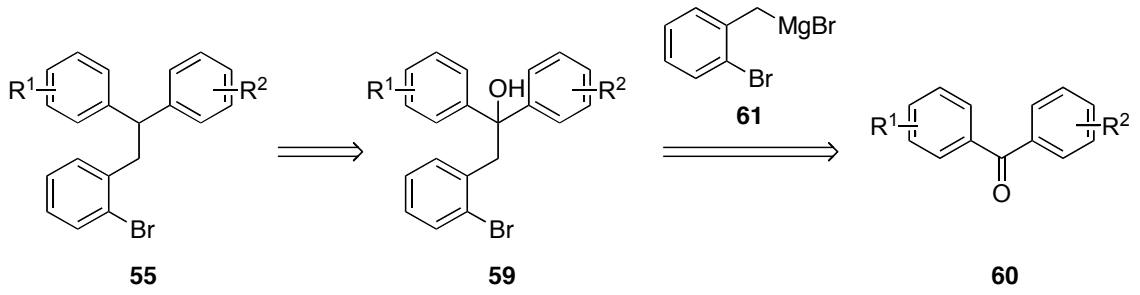
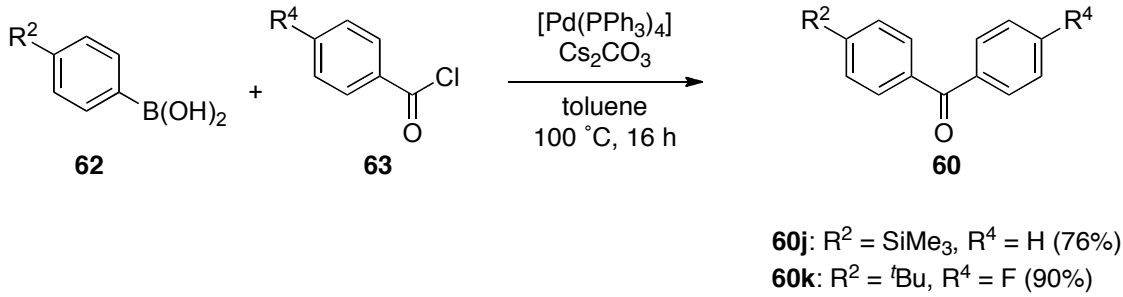


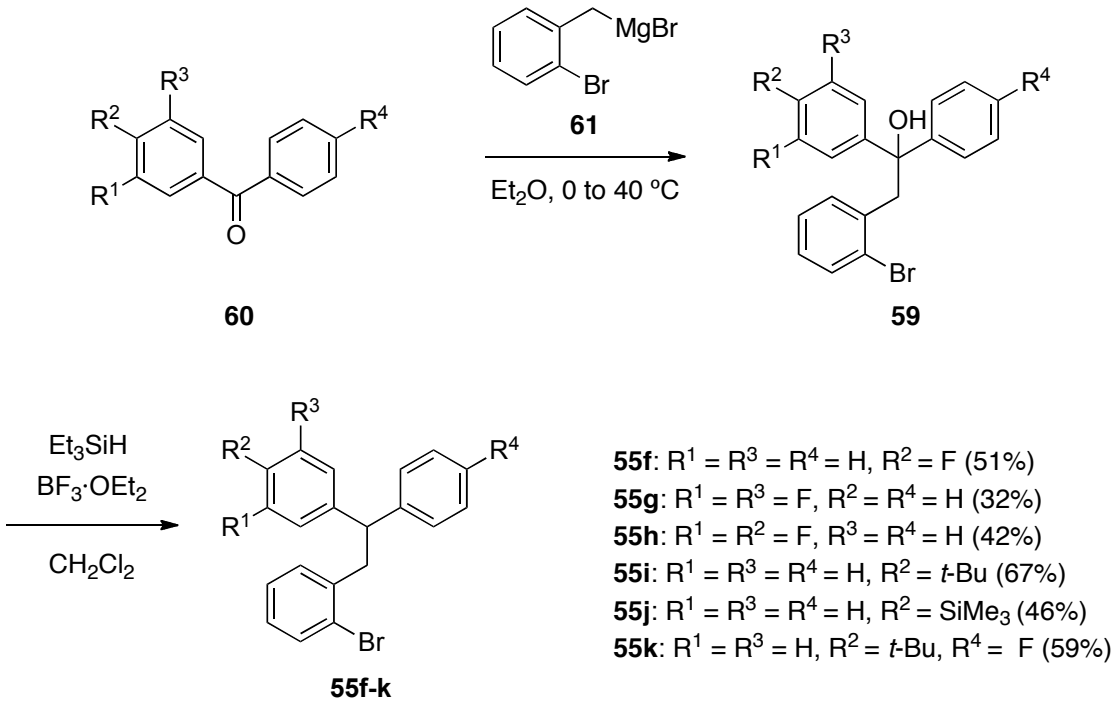
Scheme 28

4-Trimethylsilylbenzophenone **60j** and 4-*tert*-butyl-4'-fluorobenzophenone **60k** are not commercially available. Instead, they were prepared using palladium-catalyzed Suzuki cross-coupling reaction from the corresponding boronic acid derivative **62** and benzoyl chloride **63** using standard conditions (*Scheme 29*).[116]



Scheme 29

The addition of Grignard reagent **61**, prepared in situ from 2-bromobenzylbromide and magnesium, to benzophenones yielded the corresponding alcohols **59**. After the work-up and without further purification, the reduction of the alcohols was achieved with triethylsilane and $BF_3 \cdot OEt_2$ to give the desired bromoaryl compounds **55**. In this manner, six different derivatives **55f-k** were prepared in 30 to 70% overall yield (*Scheme 30*).



Scheme 30

Compounds **55** were submitted to the palladium-catalyzed direct arylation under the conditions developed by Fagnou[117] that we had already employed in our previous work.[114] These involved the use of 5 mol% of $Pd(OAc)_2$, 10 mol% of bulky phosphine ligand **58**,[118] and 3 equiv of K_2CO_3 as base at 135 ºC in DMA. Under these conditions, arylations furnished the corresponding 9,10-dihydrophenanthrenes **63**/**64**, which were obtained along with small amounts of phenanthrenes. To facilitate the determination of the ratio of regioisomers by ^{1}H NMR analysis, the crude mixtures were treated directly with DDQ to give the corresponding phenanthrenes **56**/**57** (*Scheme 31*).

117 Campeau, L.-C.; Parisien, M.; Leblanc, M.; Fagnou, K. *J. Am. Chem. Soc.* **2004**, *126*, 9186-9187.

118 Huang, X.; Anderson, K. W.; Zim, D.; Jiang, L.; Klapars, A.; Buchwald, S. L. *J. Am. Chem.*

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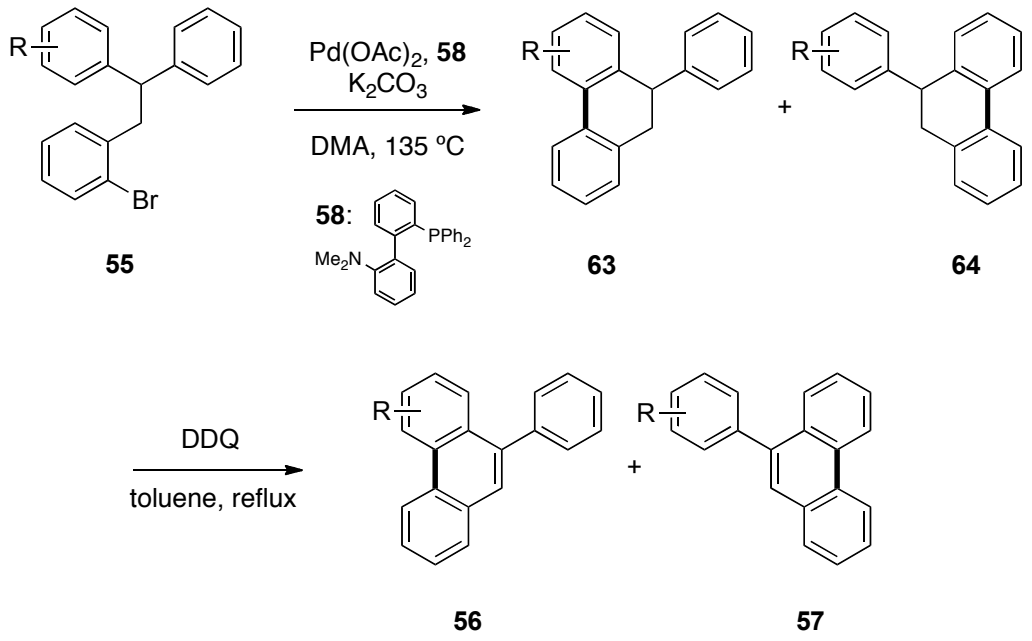
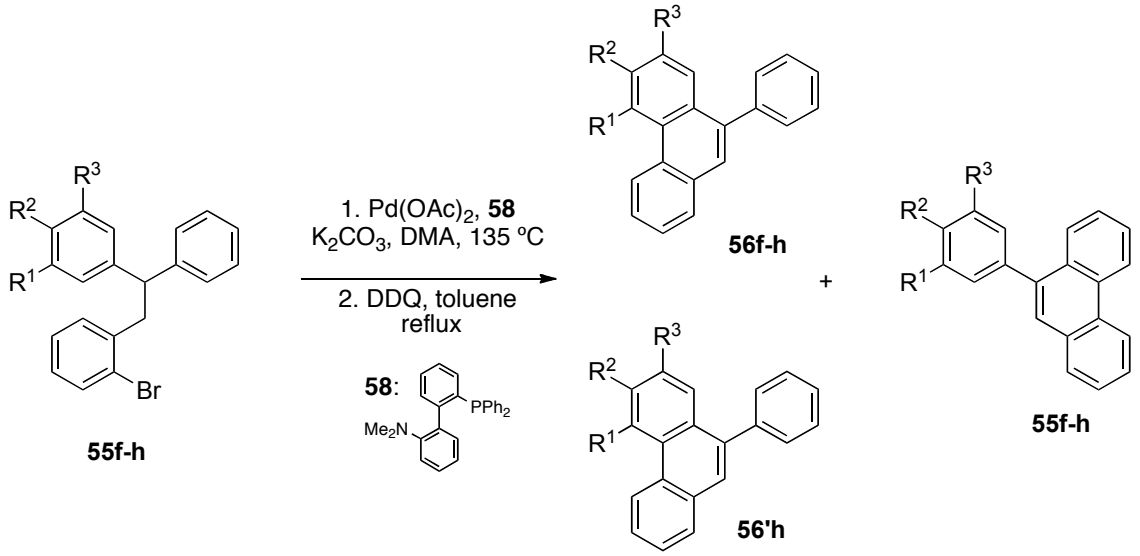


Scheme 31

Initially, the effects on the regiochemistry exerted by fluorine substituents on one of the aryl rings were studied. The results are summarized in *Table 1*.

Table 1: Pd-Catalyzed Arylation of Substrates **55f-h**.[a]



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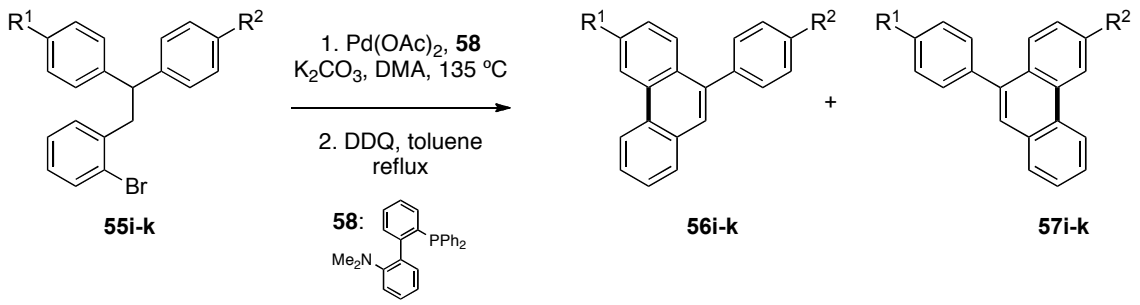
Entry	Substrate	Substituent(s)	Yield (%)	Ratio **56/57** (**56/56'/57**)
1	**55f**	R^2 = F, R^1 = R^3 = H	72	1.6:1
2	**55g**	R^1 = R^3 = F, R^2 = H	76	**19:1**
3	**55h**	R^1 = R^2 = F, R^3 = H	62	8.2:1 (6.8:1.4:1)

[a] Reactions carried out with 5 mol% of $Pd(OAc)_2$, 10 mol% of **58**, and K_2CO_3 (3 equiv) for 16 h in DMA at 135 ºC.

A single fluorine substituent in **55f** exerted a moderate control on the regioselectivity (*Table 1*, entry 1), similar to that of methoxyl, trifloromethyl, or chlorine substituents meta to the arylation site.[114] However, substrate **55g**, with fluorines substituents ortho and para to the C-H activated site (*Table 1*, entry 2), led to **56g** with an excellent regioselectivity (**56g**/**57g** = 19:1), consistent with the inductive effect of the fluorines. The regioselectivity with substrate **57h**, bearing two fluorines at different positions from the reacting site, was 8:1 (*Table 1*, entry 3). Taking into account the fact that the two reactive positions at the phenyl rings are not identical, the selectivity for the reaction ortho to the fluorine, compared to the unsubstituted aryl, is *ca*. 14:1, demonstrating the higher inductive effect of the fluorine substituent at the ortho position.

Then, we studied the effect of the electron-donating substituents on the palladium-catalyzed direct arylation in substrates **55i-k** (*Table 2*).

Table 2: Pd-Catalyzed Arylation of Substrates **55i-k**.[a]



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Entry	Substrate	Substituent(s)	Yield (%)	Ratio **56/57**
1	**55i**	R^1 = *t*-Bu, R^2= H	68	1:1.5
2	**55j**	R^1 = $SiMe_3$, R^2= H	74	1:1.3
3	**55k**	R^1 = F, R^2= *t*-Bu	81	2.3:1

[a] Reactions carried out with 5 mol% of $Pd(OAc)_2$, 10 mol% of **58**, and K_2CO_3 (3 equiv) for 16 h in DMA at 135 ºC.

The arylation of substrates **55i** and **55j** with *t*-Bu and $SiMe_3$ substituents, respectively, took place preferentially on the unsubstituted phenyl ring with moderate selectivities (*Table 2*, entries 1 and 2), which shows that the regioselectivity can be inverted with such electron-releasing groups. In agreement with a reaction proceeding preferentially on the most electron-deficient ring, which in these cases is the unsubstituted one, these results further proof our mechanistic proposal.

The arylation of substrate **55k** took place selectively at the fluorine-substituted aryl (**56k/57k** = 2.3:1; *Table 2*, entry 6). This experimental data is similar to the expected selectivity calculated from the effects of *Table 1*, entry 1 (1.6:1) and *Table 2*, entry 1 (1:1.5), showing the comparable influence of both electron-donating and electron-withdrawing groups.

In addition, we also studied the selectivity of the direct arylation in heterocyclic substrate 5*H*-indeno[1,2-*b*]-pyridine (**65**). When we applied the standard conditions at 100 ºC, as expected, reaction of **65** proceeded selectively para to the pyridine ring to afford **66** as the major regioisomer (**66**/**67** = 2.1:1) (*Scheme 32*).[119]

119 5*H*-Indeno[1,2-*b*]-pyridine **65** was prepared and submitted to arylation by Dr. Domingo

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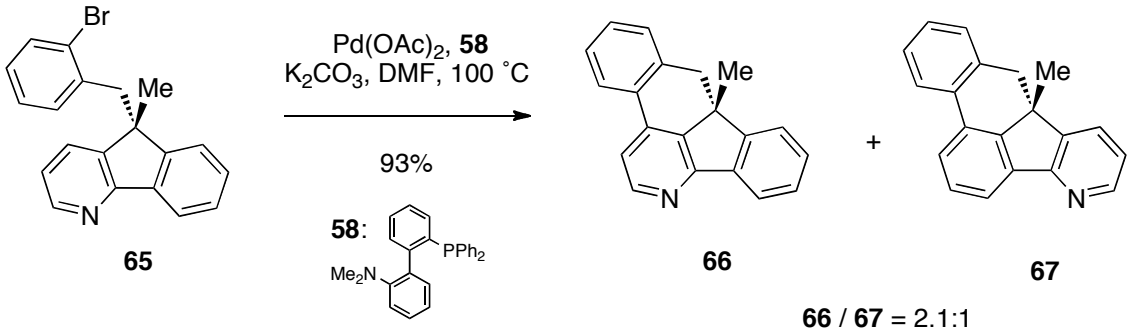

Scheme 32

In summary, with these selected examples we have demonstrated that the reaction is again favored with electron-withdrawing groups and takes place preferentially on electron-deficient aryls. The inductive effect is clearly observed with the enhanced regioselectivity that is obtained in substrates bearing fluorine atoms at the ortho position of the C-H reacting site. Moreover, we have forced the reaction to take place on the unsubstituted ring, inverting the regioselectivity by incorporating electron-releasing groups like *t*-Bu and $SiMe_3$. The final example with substrate **55k**, bearing an electron-releasing and an electron-withdrawing substituents, showed the influence of both groups on the selectivity of the reaction.

3.1.2 Effect of the Base

Previous experimental and computational studies revealed the importance of the base employed to assist the proton abstraction mechanism in the inter- and intramolecular direct arylation.[114,115,120] Consequently, we screened several organic and inorganic bidentate bases (*Table 3*) to compare their effect in the arylation of substrates **55c** and **55f**, which had already been tested with K_2CO_3.

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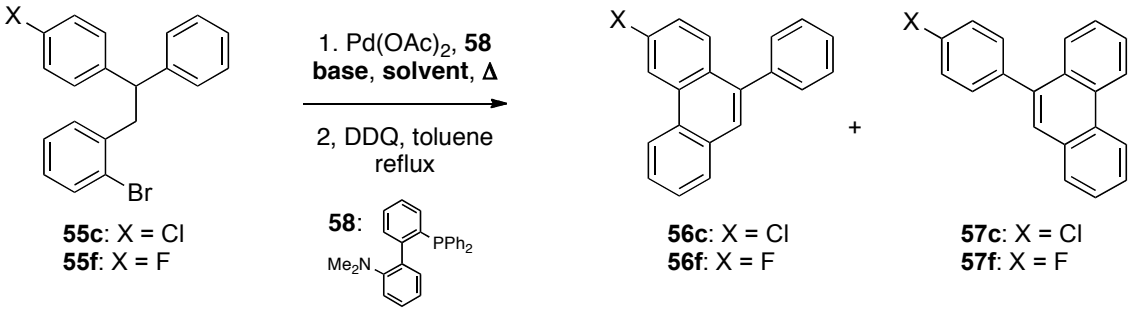
*Table 3: Effect of Base on the Pd-Catalyzed Arylation of **55c,f**.*[a]



55c: X = Cl
55f: X = F

56c: X = Cl
56f: X = F

57c: X = Cl
57f: X = F

Entry	Substrate	Base	Solvent	T (ºC)	Yield (%)	Ratio **56/57**
1	**55c**[b]	K_2CO_3	DMF	100	84	2:1
2	**55c**[b]	Et_3N	DMF	100	-	-
3	**55c**[b]	DBU	DMF	100	-	-
4	**55f**	K_2CO_3	DMA	135	72	1.6:1
5	**55f**	$KHCO_3$	DMA	135	68	1.5:1
6	**55f**	K_3PO_4	DMA	135	66[c]	1.6:1
7	**55f**	Cs_2CO_3	DMA	135	>80[c]	1.5:1
8	**55f**	Na_2HPO_4	DMA	135	-	-
9	**55f**	NaH_2PO_4	DMA	135	-	-
10	**55f**	-	DMA	135	-	-

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% **58**, and base (3 equiv) for 16 h. [b] **55c** was prepared and submitted to cyclization by Dr. Domingo García-Cuadrado. [c] Reaction time = 24 h. Yield determined by ^1H NMR.

As reported before, satisfactory results were obtained with K_2CO_3 as the base (*Table 3*, entries 1 and 4), whereas organic bases like Et_3N or DBU led to unchanged starting material (*Table 3*, entries 2 and 3).[114] Other inorganic and bidentate bases like $KHCO_3$ and K_3PO_4 were also effective and only small decreasing in the overall yield were observed (*Table 3*, entries 5 and 6). Cs_2CO_3 that usually gives better results due to its higher solubility in common organic solvents, also led to cyclized products although the reaction time required was longer (*Table 3*, entry 7), while Na_2HPO_4 and NaH_2PO_4 were not effective (*Table 3*, entries 8 and 9). A blank

even after long reaction times (*Table 3*, entry 10). It is interesting to note that the regioselectivities are largely independent from the base used, meaning that the mechanism is not dependent of the bidentated inorganic bases used.

3.1.3 Computational Studies[121]

Considering these experimental results that clearly show the influence of the base on the proton abstraction pathway and the inductive effects of substituents, in collaboration with the group of Prof. Maseras, additional DFT studies were carried out. Our aim was to study in more detail the base-assisted abstraction step and the influence of different substituents at various positions of the aryl ring.

The defining feature on the proton abstraction mechanism is that the formation of the metal-carbon bond is concerted with the breaking of the carbon-hydrogen bond, with the hydrogen being transferred to a basic center. The existence of this type of step does not fully define the mechanism, and three variations, presented in *Scheme 33*, can be postulated. Starting from the unsusbtituted model system, species **II**, resulting from the oxidative addition of [Pd(0)] to the C-Br bond, the proton can be transferred either to the bromide ligand (not assisted path, **IV**) or to another base in the media (assisted path). Moreover, the external base can either coordinate previously to the metal, displacing the bromide (intramolecular assisted path, **III**) or not (intermolecular assisted path, **V**) (see *Scheme 33*). Independently from the considered pathways, the proton abstraction evolves to palladacycle **VI** that, after suffering reductive elimination, delivers the arylated product.

121 Computational studies were carried out by Dr. Atahualpa A. C. Braga and Professor Feliu

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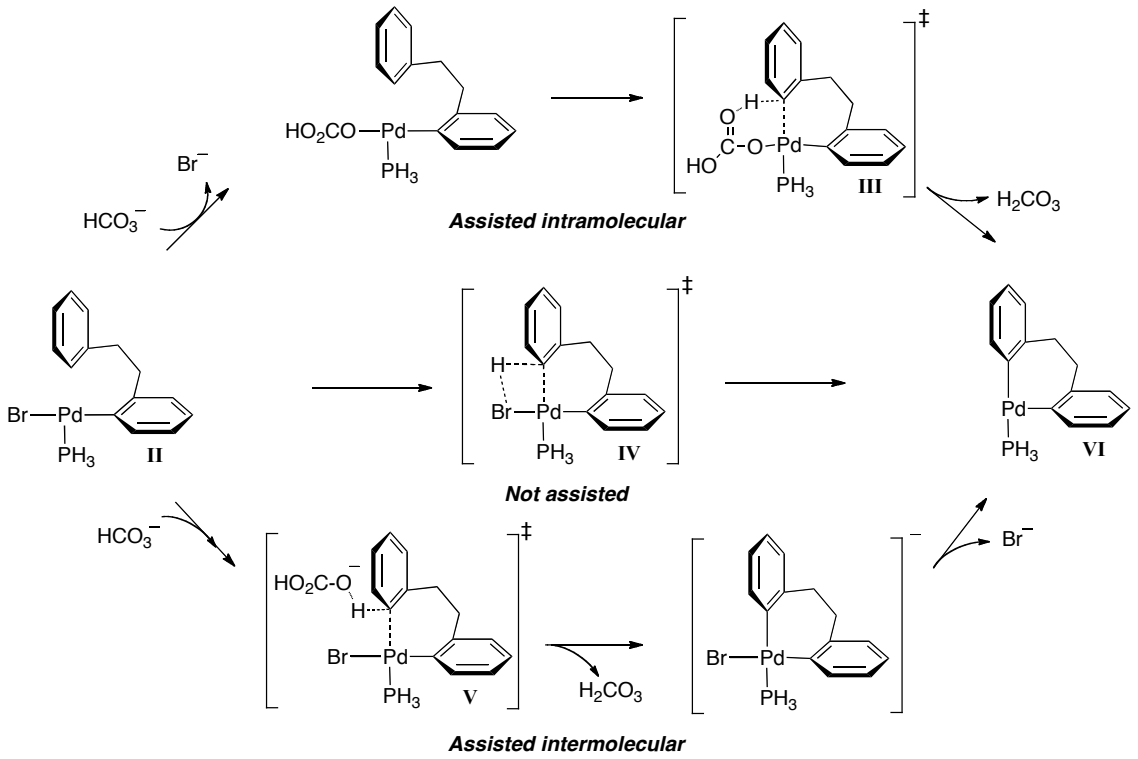

Scheme 33

Using B3LYP method, DFT calculations were carried out on [Pd(PH_3)Br(*o*-((CH_2)$_2$-C_6H_5)Ph)] **II** as a model of the experimental system, where a single phosphine ligand is considered and hydrogen atoms replaced phosphine substituents. As the base, we used bidentate hydrogen carbonate that experimentally also led to arylation (*Table 3*, entry 5).

In agreement with the observed experimental dependence of the base on the reactivity (*Table 3*), including the blank experiment carried out in the absence of base, where reaction did not occur (*Table 3*, entry 10), the unassisted process with the proton being abstracted by the bromide ligand, seems to be unlikely. The calculated free energy barrier from the oxidative addition compound **II** to the corresponding transition state **III**, for an unassisted pathway, was found to be 43.4 kcal/mol (approximately more than 20 kcal/mol higher than both assisted processes for the unsubstituted model system). However, computational data were not conclusive to determine whether intramolecular arylation mechanism goes through an intramolecular **II** (23.5 kcal/mol) or an intermolecular **IV** (17.4 kcal/mol)

assisted pathway; being the calculated energy barriers similar and acceptable for a reaction taking place at 100-135 ºC for both assisted pathways.

The effects of a wide range of substituents on substrates **II** were also calculated by DFT. The investigated substituents were identical to those used in the experimental studies in order to further verify the validity of our postulated all over mechanism. In addition, other systems were considered such as the whole series of monofluorinated and difluorinated substrates that are more difficult to access experimentally.

In agreement with experimental data, computed energy barriers were lower for the reaction with electron-deficient aryls. For instance, for the trifuoroaryl-substituted system, for both, the intra- and the inter-molecular base assisted pathways, calculated energies were 13.2 kcal/mol and 14.4 kcal/mol, around 10 kcal/mol lower than for the unsubstituted phenyl ring. In general, the calculated selectivities found were larger than the experimental values, probably due to the simplifications in the model system. Nevertheless, the overall experimental trend observed of the substituent effect on selectivity is in complete agreement with the theoretical results. Electron-withdrawing fluorine and chlorine substituents favor in all cases the reaction on the substituted aryl, while electron-releasing trimethylsilyl group drive the reaction towards the non-substituted ring. Computational data also showed that the selectivity is very sensitive to the position of the substituent in the aryl ring. Thus, the effect in the position ortho to the C-H bond being activated was considerably much larger.[115]

All these results and the mechanism we proposed is in line with later results on the intra-[113] and intermolecular[122,123] palladium-catalyzed arylation that proceeds more easily with arenes or heteroarenes bearing strongly electron-withdrawing substituents. For instance, the group of Fagnou reported the intramolecular direct

122 (a) Lafrance, M.; Rowley, C. N.; Woo, T. K.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 8754-8756. (b) Lafrance, M.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 16496-16497. (c) Lafrance, M.; Shore, D.; Fagnou, K. *Org. Lett.* **2006**, *8*, 5097-5100.

123 (a) Campeau, L.-C.; Rousseaux, S.; Fagnou, K. *J. Am. Chem. Soc.* **2005**, *127*, 18020-18021.

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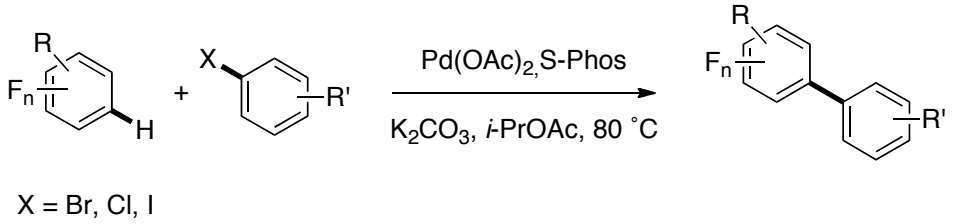
arylation of electron-deficient fluorobenzenes demonstrating the applicability of this methodology for the synthesis of biaryl systems containing fluoro aryl systems (*Scheme 34*).[122a]



Scheme 34

3.1.4 Optimization Studies[124]

Having established that direct arylation proceeds through a proton abstraction mechanism assisted by the base, we considered that the findings of new and milder reaction conditions could be later applied for the synthesis of new polycyclic aromatic hydrocarbons in a more effective manner. A main challenge in the synthesis of PAHs is their inherent difficulties on isolation, purification, and characterization. Therefore, it is crucial to find milder and regioselective conditions to avoid as much as possible side reactions and facilitate the isolation of the desired final compounds.

According to this aim, we performed an exhaustive screening of the reaction conditions including the use of a wide variety of representative organic and inorganic bases, together with the exploration of new mono- and bidentate phosphine ligands.[125]

For the optimization studies, we selected the monofluorinated substrate **55f** as a representative substrate that, under our standard arylation procedure, followed by oxidation with DDQ, yielded phenanthrenes **56f**/**57f** in good yields with an experimentally significant regioselective ratio of 1.6 to 1 (*Table 1*, entry 1).

---

124 Optimization studies of the Pd-catalyzed direct arylation reaction were carried out in collaboration with Dr. Sergio Pascual (ICIQ).

125 Pascual, S.; de Mendoza, P.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *Tetrahedron*

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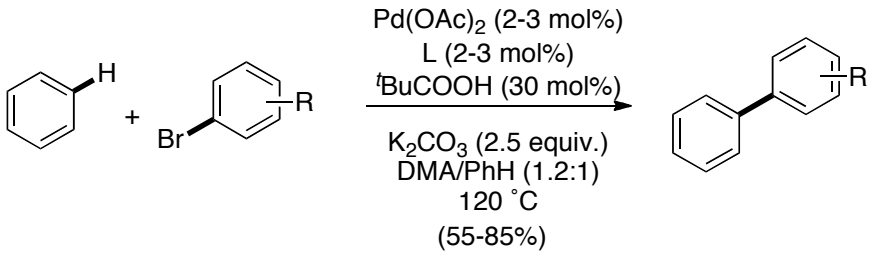
3.1.4.1 Optimizations Using Catalytic Additives

Recently, it was found in the group of Fagnou that the addition of pivalic acid as co-catalyst in the palladium-catalyzed direct arylation exhibited unprecedented enhanced reactivity.[122b] For instance, the direct arylation of unactivated arenes such as benzene can occur under relatively mild conditions by using this co-catalytic system (*Scheme 35*), while other carboxylic acids led to poorer results in this process. Experimental evidences and theoretical calculations indicate that the pivalate anion, generated in situ from substoichiometric amounts of pivalic acid and an excess of base such as potassium carbonate, is a key component for lowering the energy barrier of C-H bond cleavage. In agreement with a base assisted C-H bond activation mechanism as the rate-determining step, a significant intermolecular isotope effect of 5.5 was determined for the biaryl formation.[122b]



Scheme 35

To explore the influence of pivalic acid in our system we studied the palladium-catalyzed direct arylation on substrate **55f** with different bases (K_2CO_3, Cs_2CO_3, and KOAc) in the presence and absence of substoichiometric amounts of pivalic acid (*Table 4*).

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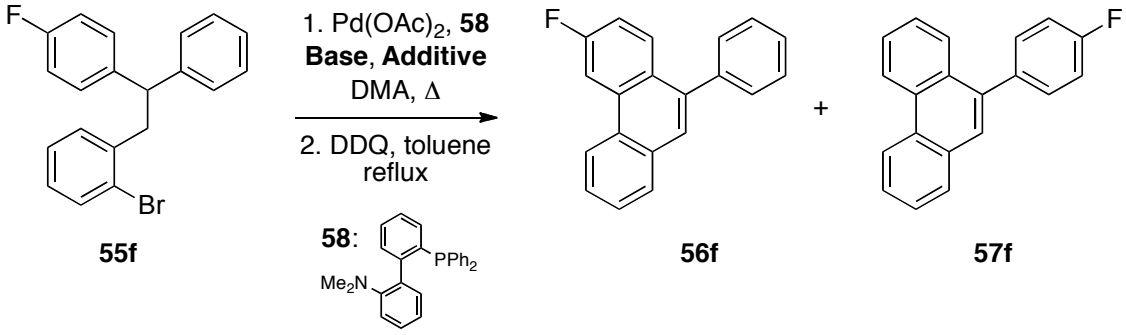
*Table 4: Pd-Catalyzed arylation of substrate **55f** with different bidentate bases in the presence and absence of pivalic acid.*[a]



Entry	Base/Additive	T (ºC)	Time (h)	Conversion (%)	Ratio **56/57** (yield %)
1	K_2CO_3	135	16	>95	1.6:1 (72)
2	K_2CO_3	100	25	92	1.7:1[b]
3	K_2CO_3/*t*-$BuCO_2H$[c]	100	4	>95	1.7:1 (79)
4[d]	**K_2CO_3/*t*-$BuCO_2H$[c]**	**100**	**4**	**>95**	**1.7:1 (86)**
5	K_2CO_3/*t*-$BuCO_2H$[c]	80	42	>95	1.5:1 (75)
6	Cs_2CO_3	135	24	>80	1.5:1
7	Cs_2CO_3/*t*-$BuCO_2H$[c]	80	42	84	1.4:1 (67)
8	KOAc	80	42	52	1.5:1[b]
9	KOAc/*t*-$BuCO_2H$[c]	80	42	65	1.5:1[b]

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% **58** and base (2.5 equiv) in DMA. Conversions were determined by ^1H NMR of the crude mixtures. [b] Isolated yield was not determined. [c] 30 mol% of pivalic acid. [d] Reaction with 5 mol% of bidentate dppf as ligand.

In the arylation of substrate **55f** with the three bidentate bases, the addition of substoichiometric amounts of pivalic acid enhanced the reactivity and, in general, the arylation could be carried out at milder temperatures or in shorter reaction times The best results were obtained in the presence of potassium pivalate, formed in situ with K_2CO_3 and pivalic acid. Thus, arylation at 100 ºC (*Table 4*, entry 3) in the presence of ligand **58** led to a 1.7:1 ratio of **56f** and **57f** in 79% yield in only 4 h. Interestingly, an 86% yield was obtained when the bidentate ligand 1,10-bis(diphenylphosphino)ferrocene (dppf) was used (*Table 4*, entry 4). Reactions with

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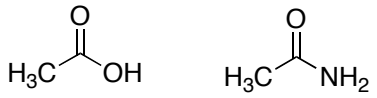
These results are in full agreement with the fact that pivalate anion is a more effective base than carbonates or acetates during the proton abstraction rate determining step. To find even more efficient bidentate bases, we decided to test nitrogen-containing primary and secondary amides (*t*-BuCONH$_2$ and *t*-BuCONHMe, respectively), which are more basic than carboxylic acids (compare pK_a values in DMSO of acetic acid and acetamide in *Figure 14*).

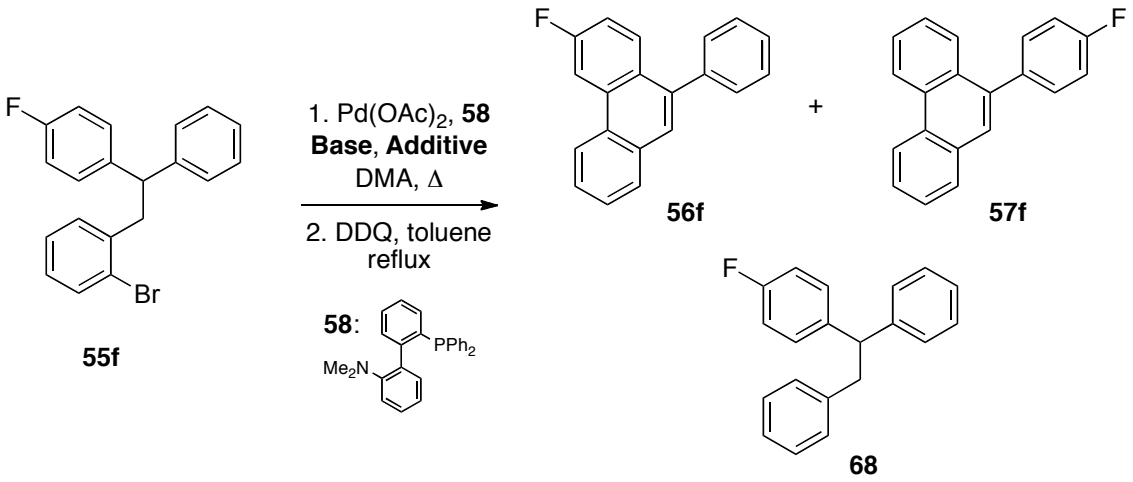


pK_a (DMSO) 12.3 pK_a (DMSO) 25.5

Figure 14: pK_a values of acetic acid and acetamide in DMSO.[126]

To deprotonate the amides and generate in situ anionic amidates, we used stronger organometallic bases like NaH or *t*-BuOK. For the catalyzed arylation, bases and amides where added in different amounts and under different conditions. However, under most of the reaction conditions, reduced product **68**, was the major compound detected in the crude mixtures (*Table 5*).

*Table 5: Pd-Catalyzed arylation of substrate **55f** with different bases.*[a]



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Entry	Base/Additive	T (ºC)	Time (h)	Conversion (%) (% **68**)	Ratio[b] **56**/**57**
1	NaH	135	52	>95 (95)	0.2:1
2	NaH/*t*-BuCONH$_2$[c]	135	52	>95 (87)	0.1:1
3	NaH/*t*-BuCONHMe[c]	135	52	>95 (87)	0.1:1
4	NaH/*t*-BuCONH$_2$[d]	135	22	55 (27)	1.7:1
5	NaH/*t*-BuCONH$_2$[e]	135	28	17 (11)	1.2:1
6	NaH/*t*-BuCONH$_2$[f]	135	28	23 (15)	1.2:1
7	*t*-BuOK	135	22	>95 (47)	1.7:1
8	***t*-BuOK /*t*-BuCONH$_2$[c]**	**135**	**22**	**>95 (20)**	**1.7:1**
9	***t*-BuOK /*t*-BuCONHMe[c]**	**135**	**22**	**>95 (13)**	**1.7:1**
10	*t*-BuOK /*t*-BuCONH$_2$[e]	135	26	56 (12)	1.6:1
11	*t*-BuOK /*t*-BuCONH$_2$[f]	135	26	38 (25)	1.4:1

[a] Reactions carried out with 5 mol% Pd(OAc)$_2$, 10 mol% **58**, and base (2.5 equiv) in DMA. Conversions and amounts of **68** were determined by ^{1}H NMR of the crude mixtures. [b] Isolated yields were not determined. [c] 30 mol% of amide added to the reaction mixture. [d] One equivalent each of amide and NaH. [e] The sodium or potassium amidate was formed from the amide (1 equiv) and base (1 equiv) at 0 ºC prior to the addition of **58** and the catalyst. [f] As *e* but with 2.5 equiv of each.

When NaH was used as the base, almost exclusive reduction of **55f** to **68** was observed (*Table 5*, entry 1). Sodium amidates formed in situ under different conditions, led to lower conversions and/or extensive reduction of **55f** (*Table 5*, entries 2 to 6). Similarly, *t*-BuOK led to significant amounts of reduction product (*Table 5*, entry 7), whereas substoichiometric amounts of primary or secondary amides with an excess of *t*-BuOK led to complete conversion of starting material with debrominated byproduct detected in lower amounts (*Table 5*, entries 8 and 9). The formation of amidates prior to the addition of palladium and ligand meant a decrease in reactivity and thus lower conversions (*Table 5*, entries 10 and 11)

These results show that the presence of stronger inorganic or organometallic bases like NaH and *t*-BuOK in the reaction mixture, necessary for the formation of active anionic amidates, give competitive dehalogenation side reaction and therefore, in general, lower yields and selectivities are accomplished.

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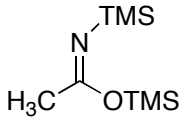
3.1.4.2 Other Nitrogen Containing Bases

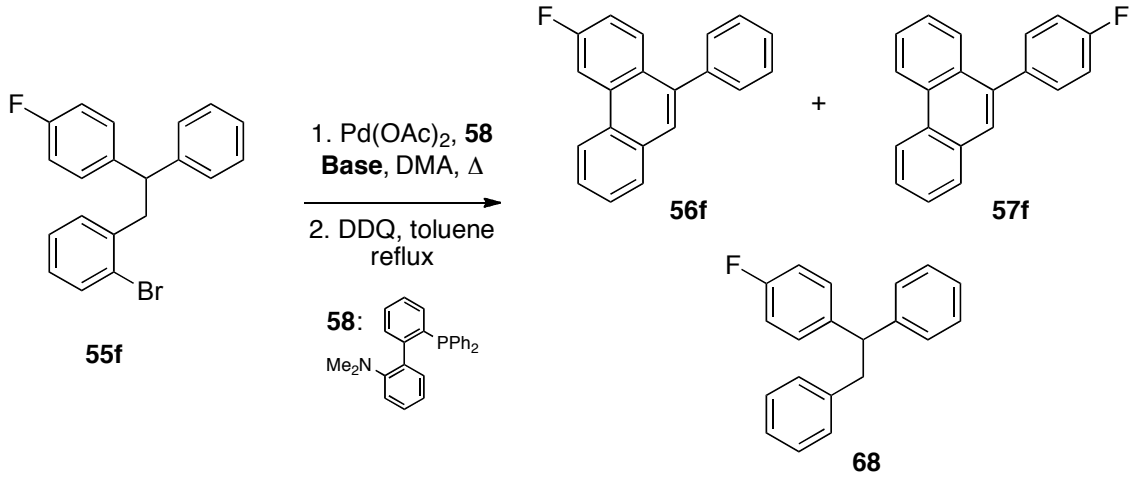
Next we explored the use of other activated nitrogen-containing bases like guanidines, ($HN=C(NMe_2)_2$ and *t*-$BuN=C(NMe_2)_2$), hexamethyldisilazane (HMDS), and imidate **69** (*Figure 15*) to evaluate the capacity of their basic nitrogen atom to abstract the proton in the key step without any need of an additional inorganic base (*Table 6*).



69

Figure 15: (Z)-Trimethylsilyl N-(Trimethylsilyl)acetamide

*Table 6: Pd-Catalyzed arylation of substrate **55f** with different nitrogen containing bases.*[a]



Entry	Ligand	Base	T (ºC)	Time (h)	Conversion (%) (% **68**)	Ratio **56**/**57** (yield %)
1	**58**	$HN=C(NMe_2)_2$	100	22	15 (5)	1.4:1[b]
2	**58**	***t*-BuN=C(NMe$_2$)$_2$**	**100**	**22**	**91 (0)**	**1.7:1 (64)**
3	**58**	Imidate **69**	135	25	-	-[b]
4	**58**	LiHMDS	100	25	-	-[b]
5	-[c]	KHMDS	80	2	55 (27)	0.8:1 (40)

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% **58**, and base (2.5 equiv) in DMA. Conversions and amounts of **68** were determined by ^{1}H NMR of the crude mixtures. [b] Yield not determined. [c] Reaction in the absence of $Pd(OAc)_2$ and ligand.

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While 1,1,3,3-tetramethylguanidine ($HN=C(NMe_2)_2$) led to poor conversion, more basic 2-*tert*-butyl-1,1,3,3-tetramethylguanidine (*t*-$BuN=C(NMe_2)_2$)[127] was an effective base for this process (*Table 6*, entries 1 and 2). When imidate **69** or LiHMDS were used, unchanged starting material was recovered even after long reaction times (*Table 6*, entry 3 and 4). Interestingly, when potassium hexamethyldisilazane was employed, reaction occurred in the absence of palladium source or ligand at lower 80 ºC temperature (*Table 6*, entry 5). Although in this case, significant amounts of reduced starting material was detected, inverted selectivity with a 0.8:1 ratio of **56f** and **57f** (40%) was obtained. This indicates that the reaction with such a strong base proceeds by a different mechanism, probably implying the formation of aryne intermediates.[128]

This last result led us to envision the use of even stronger nitrogen-containing bases. As it pointed out before, the use of highly reactive inorganic bases gave rise to undesirable dehalogenated product. Therefore, we chose neutral and metal-free phosphazene bases: *t*-Bu-P_1, *t*-Bu-P_2 and *t*-Bu-P_4 (**70-72**, shown in order of increasing basicity), known as Schwesinger bases (*Figure 16*).[129] Phosphazenes are less nucleophilic than metallic bases but extremely basic. For instance, *t*-Bu-P_4 **72** ($pK_{BH^+} = 42.7$ in MeCN) can deprotonate aromatic compounds under mild conditions.[130]

127 Raczynska, E. W.; Cyranski, M. K.; Gutowski, M.; Rak, J.; Gal, J.-F.; Maria, P.-C.; Darowska M. Duczmal, and K. *J. Phys. Org. Chem.* **2003**, *16*, 91-106.

128 See for instance: Chen, Y.; Larock, R. C. In *Arylation Reactions Involving the Formation of Arynes*; Ackermann, L., Ed.; Wiley-VCH: Weinhein, **2009**, Chapter 12, pp 401-473, and references therein.

129 (a) Schwesinger, R.; Schlemper, H. *Angew. Chem. Int. Ed.* **1987**, *26*, 1167-1169. (b) Schwesinger, R.; Hasenfratz, C.; Schlemper, H.; Walz, L.; Peters, E. M.; Peters, K.; von Schnering, H. G. *Angew. Chem. Int. Ed.* **1993**, *32*, 1361-1363. (c) Schwesinger, R.; Schlemper, H.; Hasenfratz, C.; Willaredt, J.; Dambacher, T.; Breuer, T.; Ottaway, C.; Fletschinger, M.; Boele, J.; Fritz, H.; Putzas, D.; Rotter, H. W.; Bordwell, F. G.; Satish, A. V.; Ji, G.-Z.; Peters, E.-M.; Peters, K.; von Schnering, H. G.; Walz, L. *Liebigs Ann.* **1996**, 1055-1081.

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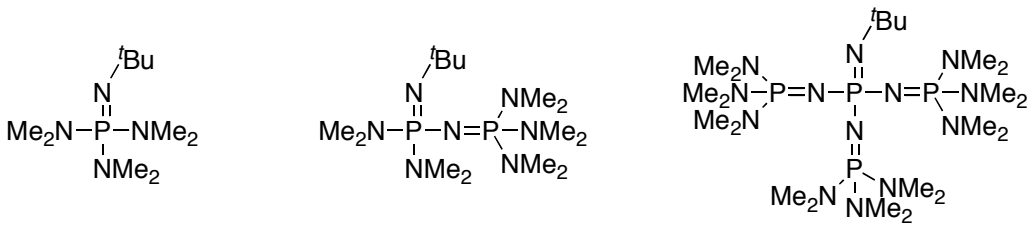
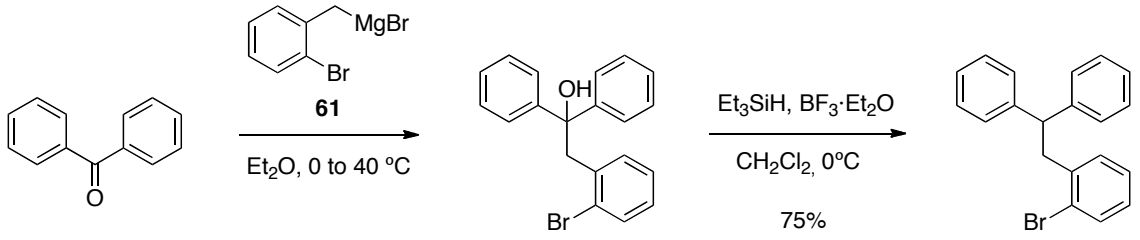


t-Bu-P_1 **70** | *t*-Bu-P_2 **71** | *t*-Bu-P_4 **72**

Figure 16: Phosphazene bases.

Preliminary studies using phosphazene bases, led to sluggish reactions and complex mixtures products. In order to simplify ^{1}H NMR analysis and determine the conversions from the crude of the reactions, we firstly prepared the non-substituted analogue of **55** that upon arylation/aromatization should deliver exclusively 9-phenylphenanthrene (**56**) as sole regioisomer. Bromoaryl compound **55l** was prepared in 75% yield following the same synthetic route as before, by addition of the Grignard reagent **61** to benzophenone followed by reduction of the resulting alcohol **59l** with Et_3SiH and $BF_3{\cdot}OEt_2$ (*Scheme 36*).



60l **59l** **55l**

Scheme 36

Bromide **55l** was submitted to arylation with the different phosphazene bases under various conditions that, upon treatment with DDQ, yielded phenanthrene **56l**. In most cases, aromatic compound **56l** was obtained with a complex mixture of other by-products (*Table 7*).

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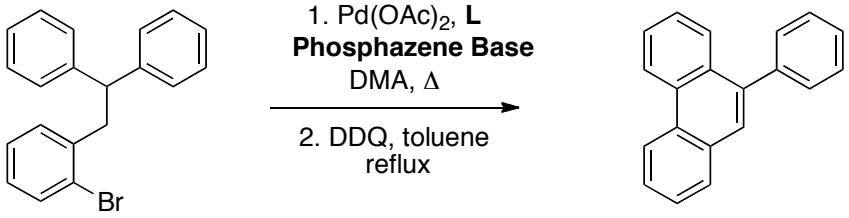
*Table 7: Pd-Catalyzed arylation of substrate **55l** with different phosphazene bases.*[a]



55l **56l**

Entry	[Pd]	Ligand	Base	T (ºC)	Time (h)	Conversion (%)	Yield (%)
1	-	-	*t*-Bu-P_4	80	4	>95	30
2	$Pd(OAc)_2$	-	*t*-Bu-P_4	60	24	>95	21
3	$Pd(OAc)_2$	-	*t*-Bu-P_4	40	53	95	28
4	-	-	*t*-Bu-P_2	135	24	0	-
5	$Pd(OAc)_2$	-	*t*-Bu-P_2	135	21	95	57
6	$Pd(OAc)_2$	**58**	*t*-Bu-P_2	135	21	95	53
7	$Pd(OAc)_2$	**dppf**	***t*-Bu-P_2**	**135**	**6**	**>95**	**66**
8	$Pd(OAc)_2$	dppf	*t*-Bu-P_2	80	22	0	-
9	-	-	*t*-Bu-P_1	135	24	0	-
10	$Pd(OAc)_2$	-	*t*-Bu-P_1	135	21	33	-[b]
11	$Pd(OAc)_2$	**58**	***t*-Bu-P_1**	**135**	**5**	**>95**	**78**
12	$Pd(OAc)_2$	dppf	*t*-Bu-P_1	135	5	>95	69

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% **58** or 5 mol% **dppf**, and base (2.5 equiv) in DMA. Conversions were determined by ^{1}H NMR of the crude mixtures. [b] Yield not determined.

When the strongest phosphazene base *t*-Bu-P_4 was used in the absence of palladium source and phosphine ligand, almost complete conversion was observed at exceptionally mild temperatures (80 ºC), while, in the presence of $Pd(OAc)_2$, reaction took place even at 60 or 40 ºC. Nonetheless, isolated yields were poor due to side reactions that led to reduced starting material together with other unidentified by-products (*Table 7*, entries 1 to 3). In contrast to strongest *t*-Bu-P_4, with *t*-Bu-P_2

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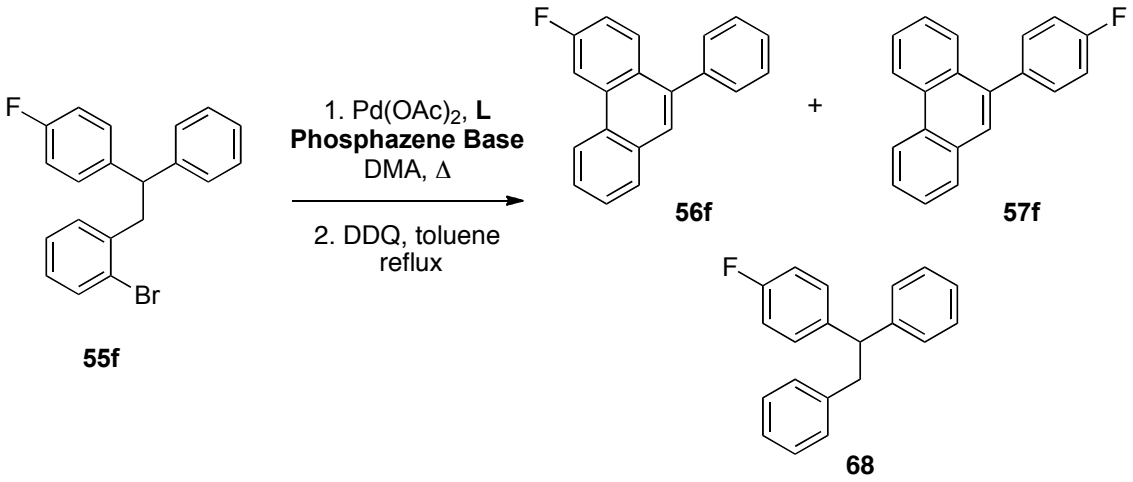
to take place (*Table 7*, compare entries 1, 4 and 7). Moderate yields were obtained with *t*-Bu-P_2 at 135 ºC when $Pd(OAc)_2$ was used in the absence of ligand (*Table 7*, entry 5). The yield was improved to 66% when dppf was used as the ligand (*Table 7*, entry 7), but reaction still required temperatures above 100 ºC (*Table 7*, entry 8). The best ligand with *t*-Bu-P_1 appeared to be **58** in which direct arylation was completed in 5 h at 135 ºC in 78% yield (*Table 7*, entry 11).

As in the case of KHMDS, the fact that direct arylation takes place with stronger oligophosphazene *t*-Bu-P_4 base in the absence of palladium, indicates that arylation proceeds through a different mechanism.[131] To investigate if an alternative mechanism competes with the base assisted proton abstraction mechanism depending on the phosphazene base used, we repeated some of the reaction conditions from *Table 7* with fluorine-containing substrate **55f** (*Table 8*).

*Table 8: Pd-Catalyzed arylation of substrate **55f** with different phosphazene bases.*[a]



131 For a recent example of transition-metal-free intramolecular arylation via benzyne

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Entry	[Pd]	Ligand	Base	T (ºC)	Time (h)	Conversion (%) (% **68**)	Ratio **56/57** (yield %)
1	-	-	*t*-Bu-P_4	80	2	>95 (0)	0:1 (15)
2	$Pd(OAc)_2$	dppf	*t*-Bu-P_4	80	4	>95 (5)	1:1.1 (30)
3	**$Pd(OAc)_2$**	**-**	***t*-Bu-P_4**	**40**	**22**	**95 (14)**	**1:1.7 (40)**
4	$Pd(OAc)_2$	-	*t*-Bu-P_2	135	20	>95 (5)	1.9:1 (64)
5	**$Pd(OAc)_2$**	**dppf**	***t*-Bu-P_2**	**135**	**5**	**>95 (5)**	**1.9:1 (69)**
6	$Pd(OAc)_2$	dppf	*t*-Bu-P_2	100	22	23 (8)	1.9:1[b]
7	$Pd(OAc)_2$	dppf	*t*-Bu-P_1	135	5	>95 (1)	1.9:1 (69)
8	**$Pd(OAc)_2$**	**dppf**	***t*-Bu-P_1**	**100**	**6**	**>95 (1)**	**1.8:1 (78)**

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 5 mol% **dppf** and base (2.5 equiv) in DMA. Conversions and amounts of **68** were determined by ^{1}H NMR of the crude mixtures. [b] Yield not determined.

Substrate **55f** reacted with *t*-Bu-P_4 base in DMA at 80 ºC for 2 h in the absence of palladium and ligand to give exclusively regioisomer **56f** in poor isolated yield (15%) (*Table 8*, entry 1). The addition of $Pd(OAc)_2$ and dppf ligand, slightly increased the yield, but still only 30% of 1:1.1 mixture of **56f/57f** could be isolated (*Table 8*, entry 2). Significantly, the reaction in the presence of $Pd(OAc)_2$ but without any ligand could be performed at lower temperatures (40 ºC) in 40% yield (compare with *Table 7*, entry 3), favoring again the arylation on the unsubstituted aryl (1:1.7 ratio) (*Table 8*, entry 3). As in the case of KHMDS, the inversion of regioselectivity with this strong base indicates that the mechanism may proceed through aryne intermediates.[128,131] In contrast, better yields (64-78%) and the expected regioselectivity for a proton abstraction mechanism favored on electron-deficient aryl rings were obtained by using phosphazene *t*-Bu-P_2 and *t*-Bu-P_1, although still temperatures above 100 ºC where required (*Table 8*, entries 4 to 8). Indeed, slightly better regioselectivities than when using carbonate bases were achieved (1.9:1), favoring the reaction to take place on the fluorine-substituted ring (compare *Table 8*, entries 4 and 8 with *Table 1*, entry 1). In accordance with a base assisted proton abstraction mechanism, these last results reflect the effectiveness in some examples of these phosphazene bases to abstract C-H acidic protons more

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selectively.

3.1.4.3 Ligand Effects

The fact that a bidentate ligand as dppf gave the best result in the presence of pivalate anion (*Table 4*, entry 4) casts doubts about the role played by this carboxylate as a ligand for palladium in the intramolecular proton abstraction event (*Scheme 33*, **III**, assisted intramolecular). Thus, if pivalate is still coordinated to palladium, an unlikely pentacoordinate [Pd(II)] intermediate bearing a diphosphine ligand would be formed. We therefore decided to examine in more detail several mono and diphosphines, as well as other ligands (*Figure 17*), in the arylation of substrate **55f** (*Table 9*). In addition, theoretical work was performed to probe the more likely base assisted intermolecular pathway when bidentate ligands are used.

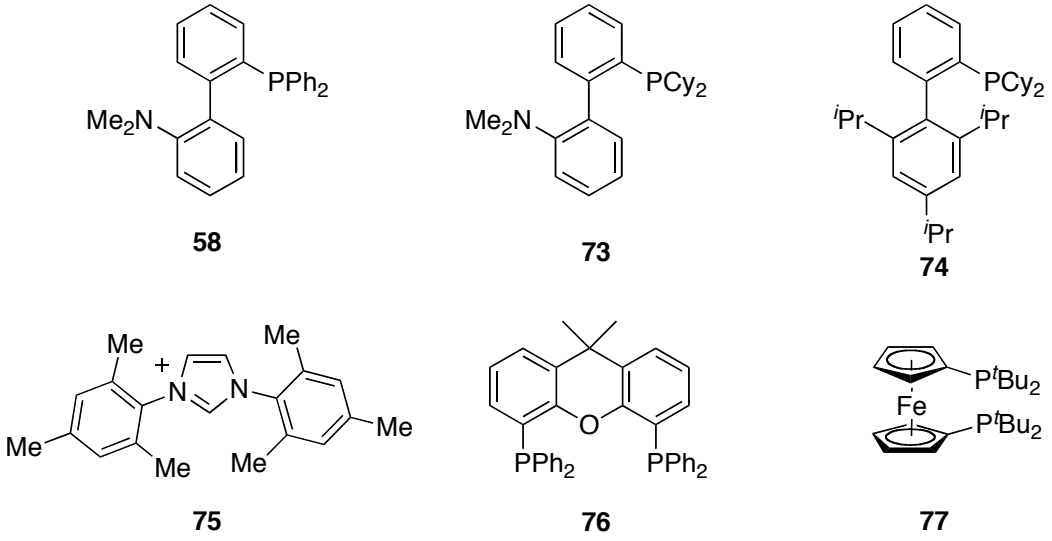

Figure 17: Ligands used for the Pd-catalyzed arylation.

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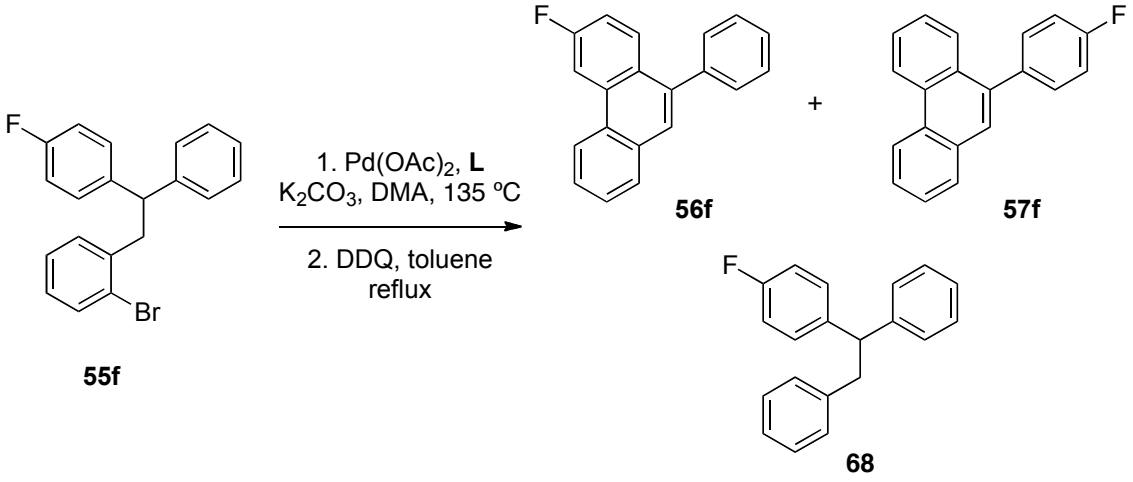
*Table 9: Pd-Catalyzed arylation of substrate **55f** with different ligands.*[a]



55f **56f** **57f** **68**

Entry	Ligand	Time (h)	Conversion (%) (% **68**)	Ratio **56**/**57** (yield %)
1	**73**	2	>95 (30)	1.5:1[b]
2	**74**	2	>95 (72)	1:1[b]
3	PCy_3	48	>95 (40)	1.5:1[b]
4	P(*o*-Tol)$_3$	21	30 (0)	1.6:1[b]
5	P*t*-Bu$_3$[c]	21	>95 (0)	1.8:1(48)
6	**75**	18	18 (0)	1.7:1[b]
7	dppf	21	>95 (-[d])	1.6:1(79)
8	**76**	**2**	**>95 (-[d])**	**1.7:1(73)**
9	**dppm**	**2**	**>95 (-[d])**	**1.7:1(77)**
10	**dppe**	**2**	**>95 (-[d])**	**1.7:1(72)**
11	dppp	2	>95 (-[d])	1.7:1(59)
12	**77**	2	>95 (-[d])	1.7:1(47)

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% of monodenate **L** or 5 mol% of bidentate $\mathbf{L_2}$, and K_2CO_3 (2.5 equiv) in DMA at 135 ºC. Conversions and amounts of **68** were determined by ^{1}H NMR of the crude mixtures. [b] Isolated yield not determined. [c] The HBF_4 salt was used. [d] Traces (<5%) of **68** were detected; dppm = bis(diphenylphosphino)methane; dppe = 1,2-bis(diphenylphosphino)ethane; dppp = 1,3- bis(diphenylphosphino)propane.

Under our standard reference conditions, with $Pd(OAc)_2$, K_2CO_3 in DMA at 135 ºC,

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monophosphines **73** and **74**,[132] which are structurally similar to **58**, led to extensive reduction (**68**) (*Table 9*, entries 1 and 2). Other monophosphine ligands or imidazolium salt IMes (*N*,*N'*-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene, **75**), were neither effective and led to poor conversion or moderate yields (*Table 9*, entries 3 to 6). In contrast, bidentate phosphines like dppf, xantphos (**76**),[133] dppm, dppe, dppp, and ferrocenyldiphosphine (**77**) in general led to faster reactions (conversions > 95 in 2 h) and with satisfactory yields (47-79%) (*Table 9*, entries 7 to 12).

These results show that diphosphines are excellent ligands for this transformation. Moreover, although it has been shown that **76** can behave as a *cis*- or *trans*-chelating ligand with [Pd(II)],[134,135] the similar behavior displayed by Xantphos (**76**) and more simple diphosphines such as dppm and dppe suggests that **76** coordinates in a *cis* fashion to palladium in this reaction (*Figure 18*).

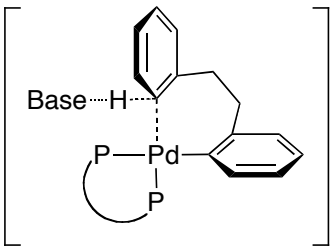

Figure 18: cis-Coordination of bidentate ligands in the intermolecular base assisted proton abstraction mechanism.

For bidentate phosphine ligands, the intramolecular base-assisted proton abstraction seems unlikely because it would require the breaking of one of the Pd-P bonds. We

132 (a) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685-4696. (b) Barder, T. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 5096-5101.

133 Kranenburg, M.; van der Burgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Organometallics* **1995**, *14*, 3081-3089.

134 *cis*-Chelation of **76** Pd(II): van Haaren, R. J.; Goubitz, K.; Fraanje, F.; van Strijdonck, G. P. F.; Oevering, H.; Coussens, B.; Reek, J. N. H.; van Leeuwen, P. W. N. M. *Inorg. Chem.* **2001**, *40*, 3363-3372.

135 *trans*-Chelation of **76** to Pd(II): (a) Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Acc. Chem. Res.* **2001**, *34*, 895-904. (b) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**,

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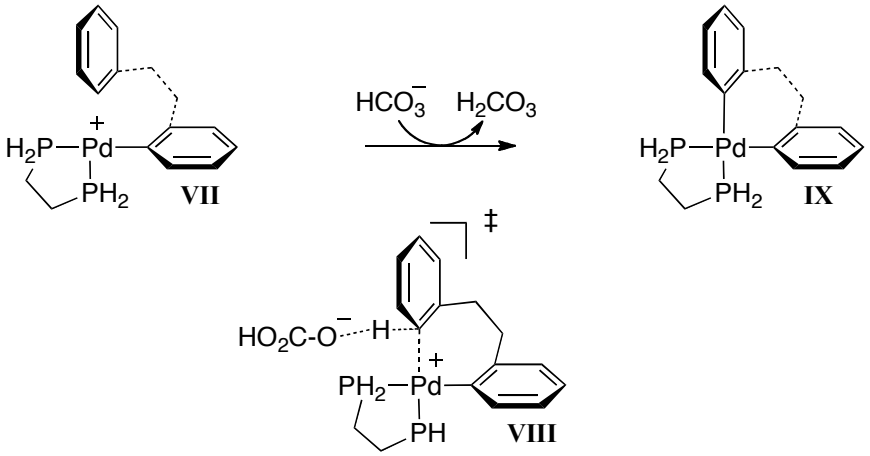
carried out a new series of DFT studies on the reaction mechanism to confirm the seeming similarity between our previous results with monodentate phosphine ligand (see *Scheme 33*)[114,115] and those found with bidentate phosphines. Accordingly, we studied the intermolecular proton abstraction mechanism for the arylation reactions with bidentate phosphine model system ($H_2PCH_2CH_2PH_2$) in the transformation of **VII** into **IX** (*Scheme 37*) in order to compare the results with the previous calculations.



transition state for the assisted intermolecular proton abstraction with bidentate phosphines

Scheme 37

Similar energetic barriers were found for the intermolecular process with monodentate and bidentate ligand system through **V** (see *Scheme 33*) and **VIII** transition states (*Scheme 37*), respectively. Thus, although addition of pivalic acid has a beneficial effect in many cases, the fact that the arylation reaction also proceeds satisfactorily and with comparable energetic barriers with palladium complexes bearing bidentate diphosphine ligands suggest that, in these cases, the base acts externally and abstracts the proton in an intermolecular fashion.[125]

To determine whether when using bidentate phosphines, the rate determining step of the reaction is the C-H activation or alternatively, there is a ligand dissociation or ligand exchange step that also interferes in the rate of the reaction, we repeat the arylation of deuterated substrate **55e** with bidentate dppf ligand. Under the standard conditions, using with $Pd(OAc)_2$, K_2CO_3 and dppf an intramolecular isotope effect

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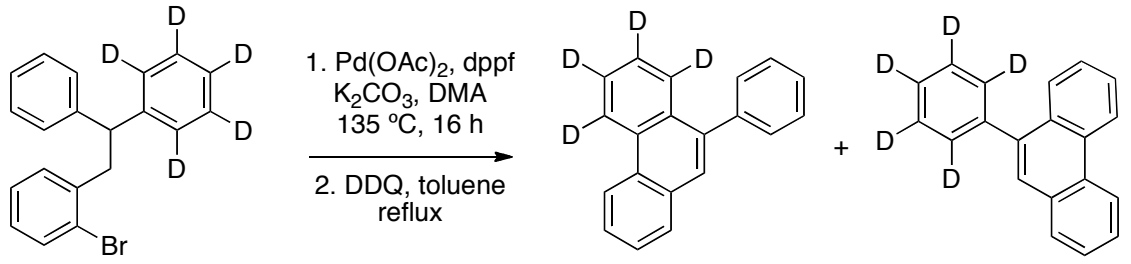
value is almost identical to that found using ligand **58** ($k_H/k_D = 5.0$) at this temperature (135 ºC),[114,115] which indicates that in the presence dppf the rate determining step is also the C-H bond cleavege.



55e **56e** **57e**

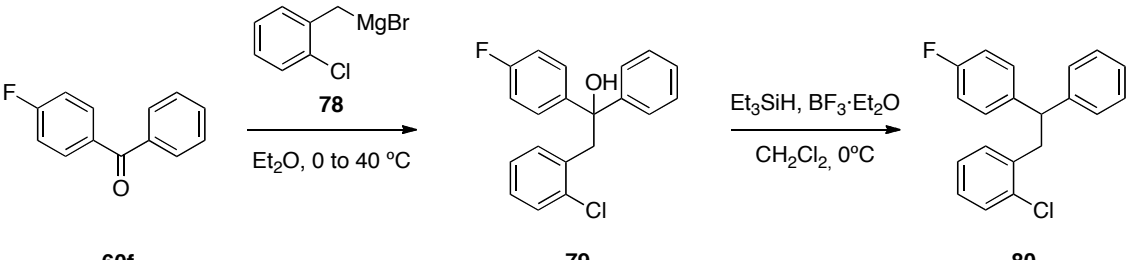
Scheme 38

3.1.5 New Substrates

Further work on this topic was focused on the study of different substrates replacing aryl bromide with aryl chloride or triflate, which are also known to be effective in the direct arylation reaction.[88,89,91,92] While aryl chlorides have especial interest in industrial applications, aryl triflates can be readily obtained from synthetically accessible OMe precursors, which also makes them very useful in synthetic applications.

3.1.5.1 Aryl Chlorides

Aryl chloride **80**, bearing a fluorine-substituted aryl ring, was prepared using the same procedure as for the bromide analogue **55f**, but starting with 2-bromobenzyl-1-chloride. Thus, the addition of the magnesium derivative **78**, prepared in situ, to fluorobenzophenone gave the corresponding tertiary alcohol **79** that after reduction, led to the desired aryl chloride derivative **80** in 60% yield over the two steps (*Scheme 39*).



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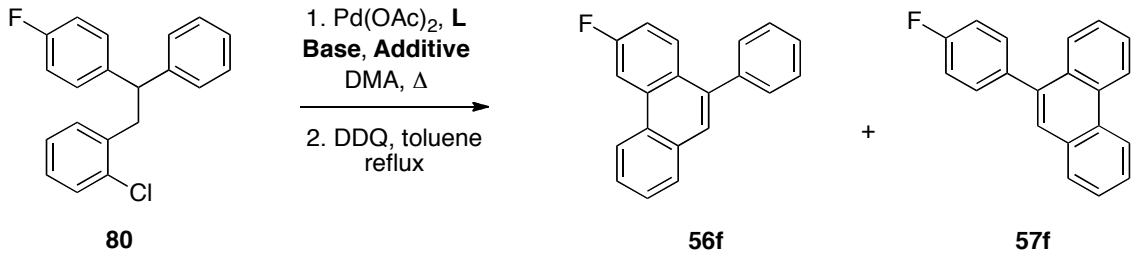
Scheme 39

Taking into account our optimization studies, we examined the palladium-catalyzed direct arylation on chloride substrate **80** with some of the catalytic systems that previously had given us the best results (*Table 10*).

*Table 10: Pd-Catalyzed arylation of aryl chloride **80** under different conditions.*[a]



80 **56f** **57f**

Entry	Ligand	Base/Additive	T (ºC)	Time (h)	Conversion (%)	Ratio **56/57**
1	**58**	**K_2CO_3**	**150**	**67**	**65**	**1.5:1**[b]
2	**58**	K_2CO_3/*t*-$BuCO_2H$[c]	150	48	27	1.7:1[b]
3	dppf	K_2CO_3	150	24	0	-
4	dppe	K_2CO_3	150	24	0	-
5	Xantphos	K_2CO_3	150	24	0	-
6	**58**	*t*-Bu-P_1	150	48	26	1:1 [b]

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% **58** or 5 mol% for bidentate $\mathbf{L_2}$, and base (2.5 equiv) in DMA. Conversions were determined by ^{1}H NMR of the crude mixtures. [b] Yield not determined. [c]

Direct arylation of aryl chlorides, as expected, required higher temperatures (150 ºC) and complete conversion of the starting material could not be achieved with the catalytic systems essayed even after long reaction times (*Table 10*). The best conversion was obtained when using **58** as the ligand and K_2CO_3 as the base but, still and all, arylation required long reaction times (65% of conversion after 67 h, *Table 10*, entry 1). Addition of pivalic acid did not enhanced reactivity and after 48 h only 27% of conversion was observed (*Table 10*, entry 2). By changing the ligand to bidentate phosphines, like dppf, dppe, or Xanthphos, no reaction occurred after 24 h (*Table 10*, entries 3 to 5) whereas, *t*-Bu-P_1 led again to poor conversion

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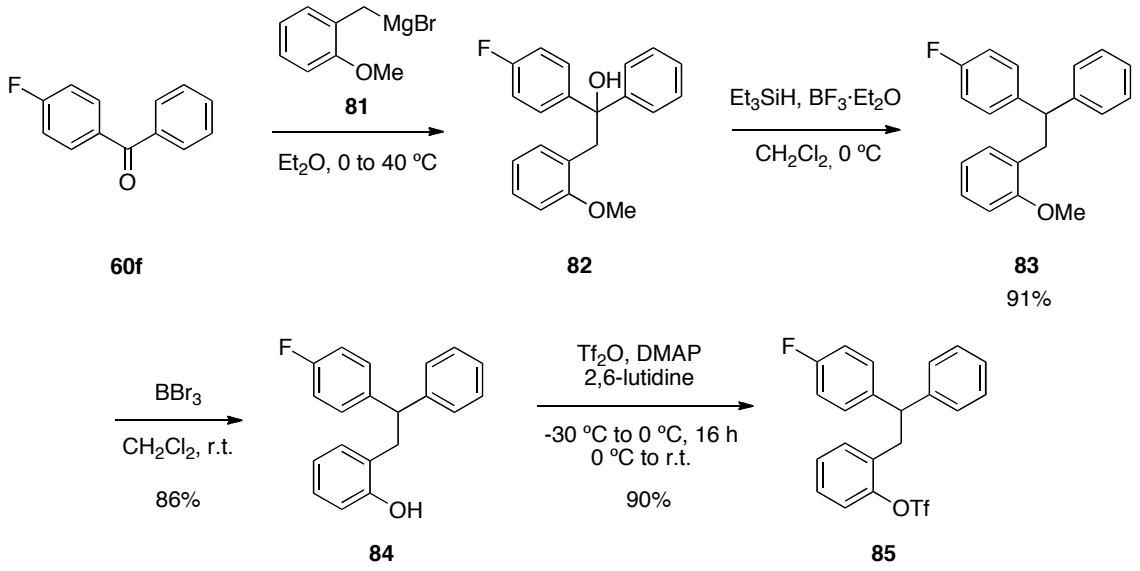
after long reaction time (*Table 10*, entry 6). Notice that regioselectivities were similar to those obtained with the bromide starting material (1.7-1.5:1), indicating that the same proton abstraction mechanism is taking place, except when phosphazene was used (1:1).

3.1.5.2 Aryl Triflates

Aryl triflate precursor **85** was prepared in a four step synthesis with a 48% overall yield, as shown in *Scheme 40*. First, methoxy derivative **83** was prepared using the same addition/reduction procedure as before in a 62% yield, starting with commercially available 1-(bromomethyl)-2-methoxybenzene, which reacted in situ with Mg to form **81**, and 4-fluorobenzophenone (**60f**). Demethylation with BBr_3 afforded the corresponding phenol **84** in good yield (86%) that was followed by triflation. Under standard conditions, using triflic anhydride, 2,6-lutidine in DMAP gave the desired aryl triflate **85** in 90% yield.



Scheme 40

When aryl triflate **85** was submitted to the cyclization/aromatization sequence, in addition to arylated phenanthrenes, phenol derivative **84** was detected in most of the reactions (*Table 11*).

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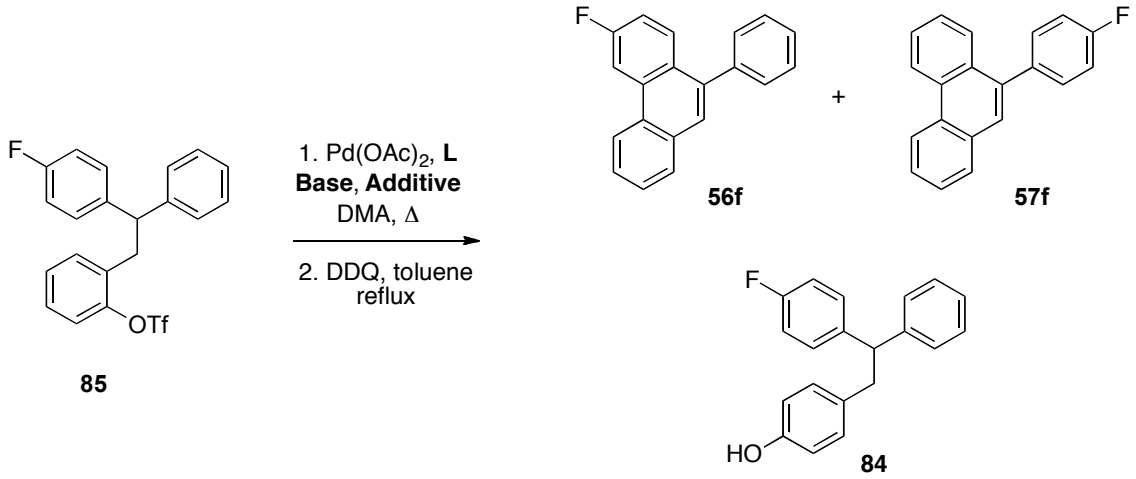
*Table 11: Pd-Catalyzed arylation of aryl triflates **85** under different conditions.*[a]



Entry	Ligand	Base/Additive	T (°C)	Time (h)	Conversion (%) (% **84**)	Ratio **56**/**57** (yield %)
1[b]	-	DBU/LiCl[c]	140	14	>95 (>95)	-[d]
2	-	DBU/LiCl[c]	100	18	>95 (>95)	-[d]
3[b]	PPh_3[e]	DBU/LiCl[c]	140	14	>95 (>95)	-[d]
4	**58**	K_2CO_3	135	18	>95 (50)	-[d]
5	**58**	**K_2CO_3**	**100**	**24**	**76 (traces)**	**1.6:1(60)**
6	**58**	K_2CO_3	60	48	43 (0)	1.5:1[d]
7	**58**	K_2CO_3/*t*-$BuCO_2H$[c]	60	48	10 (0)	1.5:1[d]
8	dppf	K_2CO_3/*t*-$BuCO_2H$[c]	100	29	traces	-[d]
9	-	*t*-Bu-P_4	60	6	>95 (>95)	-[d]
10	-	*t*-Bu-P_2	135	14	>95 (58)	-[d]
11	-	*t*-Bu-P_1	135	48	>95 (20)	1.6:1[d]

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% **58** or 5 mol% dppf and base (2.5 equiv) in DMA. Conversions and amounts of **84** were determined by ^1H NMR of the crude mixtures. [b] 10 mol% of $PdCl_2(PPh_3)_2$ [c] 12 equiv of DBU and 3 equiv of LiCl in DMF. [d] Yield not determined. [e] 40 mol% of PPh_3.

The standard conditions for the palladium-catalyzed direct arylation of aryl triflates in the context of PAHs synthesis, are $PdCl_2(PPh_3)_2$ as catalyst, DBU as base in the presence of LiCl in DMF.[88,89] Applying these conditions, compound **85** led exclusively to phenol **84** (*Table 11*, entry 1 to 3). Under the optimized conditions

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crude mixture was composed by phenol (*Table 11*, entry 4). Higher selectivity was obtained lowering the temperature to 100 ºC, and although only 76% of conversion was achieved, 60% of regioisomers **56f/57f** were isolated in a 1.6:1 ratio (*Table 11*, entry 5). When temperature was decreased to 60 ºC, conversion dropped to 43% without any increase in the regioselectivity (*Table 11,* entry 6), while addition of pivalic acid at the same temperature also reduced considerably the reactivity (*Table 11*, compare entries 6 and 7). The use of phosphazene bases, in general, led to high amounts of phenol or required long reaction times (*Table 11*, entries 9 to 11).

These results show that in this system, aryl chlorides are not as effective as bromine substrates and still further optimization studies should be carried out to find new conditions that allow the reaction to proceed under less drastic conditions. For triflate substrate **85**, although arylation does not proceed under the commonly employed condition for the synthesis of PAHs, we have shown that under the optimized conditions for aryl bromides **55**, triflates can also undergo arylation reaction and by lowering the temperature the formation of free phenol **84** can be almost avoided.

3.1.6 Investigation on the Enantioselective Arylation Reaction

The arylation of dialkylated fluorene derivatives, in which dehydrogenation cannot occur after cyclization, was reported earlier in our group. In the presence of palladium catalyst, either a quaternary stereogenic centre or, in the case of dibromobenzyl substituted fluorene, a spiro derivative, with axial chirality were formed.[110]

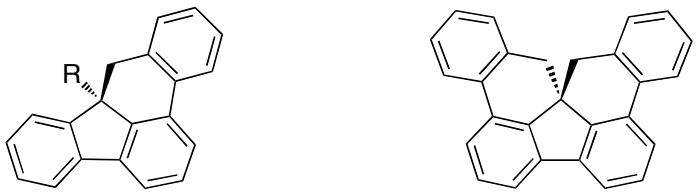

Figure 19: Disubstituted fluorenes that after arylation present a stereogenic centre or axial chirality.

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We wanted to investigate if the use of chiral phosphine ligands (Josiphos or BINAP, *Figure 20*) could induce chirality promoting an enantioselective version of this direct arylation.

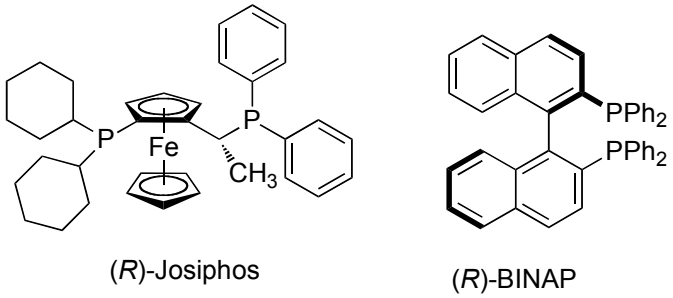
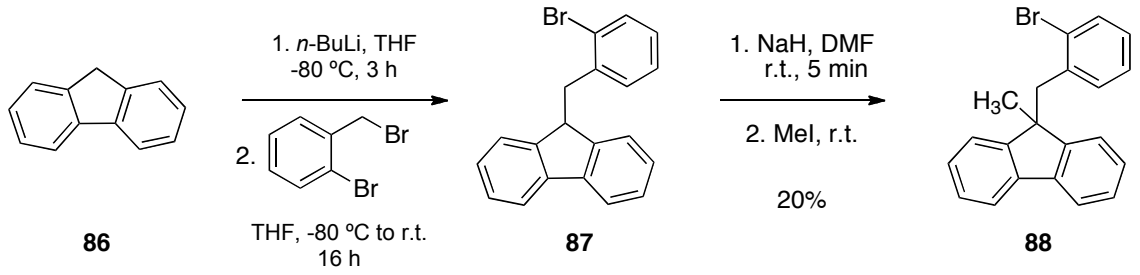


Figure 20: Enantiomerically pure ligands used for the palladium-catalyzed direct arylation.

As previously reported, dialkylated fluorenes can be prepared by a double deprotonation/alkylation sequence. In the case of 9-(2-bromobenzyl)-9-methyl-9*H*-fluorene (**88**), alkylation with 2-bromobenzylbromide was followed by methylation (*Scheme 41*). Deprotonation of fluorene **86** was carried out with *n*-BuLi at low temperature, while anion formation of substituted fluorene **87** was done with NaH in an ultrasound bath, following the described procedure for a closely related substrate.[110]



Scheme 41

Substrate **88** was submitted to the palladium-catalyzed direct arylation using firstly racemic BINAP ligand and later with enantiomerically pure (*R*)-BINAP and (*R*)-Josiphos (*Table 12*).

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Table 12: Pd-Catalyzed arylation of dialkylated fluorene.[a]

88 **89**

Entry	Ligand	Base	T (°C)	Time (h)	Conversion (%)	Yield (%)	*ee* (%)
1	*rac*-BINAP	K_2CO_3	100	48	60	-[b]	-
2	*rac*-BINAP[c]	K_2CO_3	135	24	90	-[b]	-
3	(*R*)-BINAP[d]	K_2CO_3	135	60	90	79[e]	0
4	**(*R*)-Josiphos[c]**	**K_2CO_3**	**135**	**6**	**>95**	**90**	**0**

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 5 mol% of $\mathbf{L_2}$ and base (2.5 equiv) in DMA. Conversions were determined by ^{1}H NMR of the crude mixtures. [b] Yield not determine. [c] 10 mol% of $Pd(OAc)_2$ and 10 mol% of $\mathbf{L_2}$. [d] 20 mol% of $Pd(OAc)_2$ and 20 mol% of bidentate phosphine. [e] Yield determinated by ^{1}H NMR.

For pro-quiral substrate **88**, reactivity appeared to be low and when *rac*-BINAP was used at 100 ºC, after 48 h only 60% of conversion was achieved (*Table 12*, entry 1). Using 10 mol% of catalytic Pd-ligand system at 135 ºC reaction reached 90% of conversion with racemic BINAP (*Table 12*, entry 2). Under similar conditions, the reaction was performed with enantiomerically pure (*R*)-BINAP, but, although satisfactory yield was achieved (79%), the product did not show any enantiomeric excess (*Table 12*, entry 3). Using chiral (*R*)-Josiphos, reactivity was enhanced to 90% yield, but again no enantiomeric excess was observed (*Table 12*, entry 4).

Double bromobenzyl alkylated fluorene **91** was prepared using the described procedure through a stepwise alkylation sequence with *ortho*-bromobenzyl bromide. Cyclization for the synthesis of spiro polycycic aromatic hydrocarbon **91** originally proceed in 68% yield with $Pd(OAc)_2$, K_2CO_3 and Bu_4NBr at 130 ºC in 24 h.[110] We performed the arylation reaction at 135 ºC, with racemic and enantiomerically pure previously used phosphine ligands (*Table 13*).

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Table 13: Pd-Catalyzed arylation of dialkylated fluorene.[a]

90 **91**

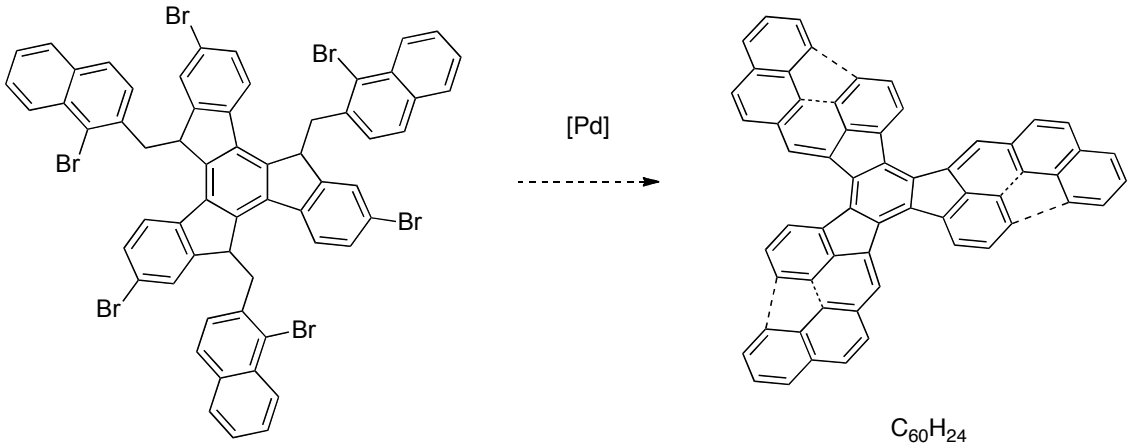
Entry	Ligand	Time (h)	Conversion (%)	Yield (%)	ee (%)
1	BINAP	40	>95	60[b]	-
2	(*R*)-BINAP[c]	60	90	86	0
3	**(*R*)-Josiphos**	**6**	**>95**	**91**	**0**

[a] Reactions carried out with 10 mol% $Pd(OAc)_2$, 10 mol% of $\mathbf{L_2}$ and K_2CO_3 (2.5 equiv) in DMA at 135 ºC. Conversions were determined by ^{1}H NMR of the crude mixtures. [b] Yield determinated by ^{1}H NMR. [c] 20 mol% of $Pd(OAc)_2$ and 20 mol% of $\mathbf{L_2}$.

Spiro compound **91** could be obtained by double arylation using racemic BINAP, enantiomerically pure (*R*)-BINAP or (*R*)-Josiphos from moderate to excellent yields (60-91%) (*Table 13*). Again, no asymmetric induction was obtained when employing enantiopure ligands.

3.2 Palladium Catalyzed Arylation for the Synthesis of Non-Planar PAHs[136]

Taking into account our previous optimization studies where we found improved conditions for the palladium-catalyzed direct arylation and the precedents in our groups for the synthesis of crushed fullerenes,[9,95] we planed to apply the new conditions on the synthesis of polyaromatic compounds. Initially, we explored the arylation conditions in model systems to latter apply the best results on the synthesis of larger polyaromatic compounds and crushed fullerenes. Further on, we planned to synthesized hexabromotruxene **92** that potentially could undergo hexacyclization to formed $C_{60}H_{24}$, **93**, crushed fullerene in a single step (*Scheme 42*). Interestingly, Shevlin and co-workers, in their studies on the mechanism of C_{60} fullerene formation, already proposed this $C_{60}H_{24}$ polycyclic compound as a possible intermediate during fullerene formation.[137] Nevertheless, its synthesis and characterization has not been reported until now.



92 **93**

Scheme 42

As a prelude to the more complex synthesis of larger polyaromatic hydrocarbons, initially we applied our recently explored arylation conditions to simplified model systems based on bromoaryl functionalyzed fluorenes **87**/**94**, as shown in *Scheme 43*, which have already the carbon framework of C_{60} fullerene.

136 Applications of the Pd-catalyzed direct arylation for the synthesis of PAHs were carried out in collaboration with Dr. Sergio Pascual (ICIQ).

137 Chang, T.-C.; Naim, A.; Ahmed, S. N.; Goodloe, G.; Shevlin, P. B. *J. Am. Chem. Soc*. **1992**,

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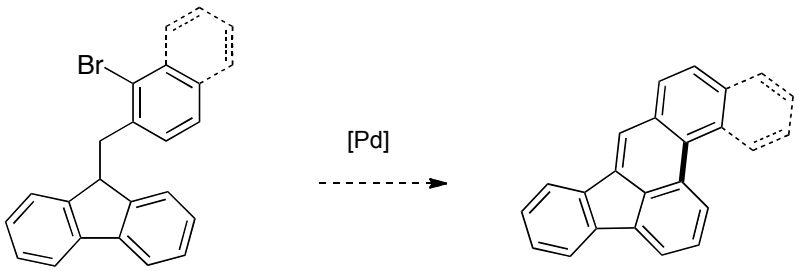

87/94 **95/96**

Scheme 43

3.2.1 Bromobenzyl Fluorene

In our research group, it has already been reported the palladium-catalyzed cyclization of 9-(bromobenzyl)-9*H*-fluorene (**87**) to give benz[*e*]acephenanthrylene (**95**). When $Pd(OAc)_2$ (5 mol%) was used in the presence of 3 equiv of Bu_4NBr and K_2CO_3 (8 equiv.) in DMF (130 °C, 48 h) an optimized 52% yield of arylated **95** was obtained.[110] Noteworthy, with 2-methoxyfluorene derivatives, reactions were sluggish and the replacement of Bu_4NBr by LiI additive appeared to be essential for product isolation, while addition of PPh_3 or $AsPh_3$ ligands led to poorer results.[110]

Following the described procedure,[110] we prepared bromobenzyl derivative **87** and submitted it to some of our arylation conditions that we found effective in the biaryl system **55f**. The results of the palladium-catalyzed arylation on bromobenzyl fluorene **87** derivative are depicted in *Table 14*.

*Table 14: Pd-Catalyzed arylation of bromobenzyl fluorene **87**.*[a]

87 **95**

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Entry	Ligand	Base/Additive	T (°C)	Time (h)	Conversion (%)	Yield (%)
1	**58**	K_2CO_3	80	20	>95	-[b]
2	**58**	K_2CO_3/*t*-$BuCO_2H$[c]	80	26	>95	58
3	**58**	K_2CO_3	60	48	>95	62
4	**58**	**K_2CO_3/*t*-$BuCO_2H$[c]**	**60**	**24**	**>95**	**73**
5	dppf	K_2CO_3	80	20	>95	-[b]
6	dppf	K_2CO_3/*t*-$BuCO_2H$[c]	80	26	>95	40[d]
7	dppf	K_2CO_3	60	24	>95	71
8	dppf	K_2CO_3/*t*-$BuCO_2H$[c]	60	24	>95	59
9	dppf	K_2CO_3	40	26	>95	-[b]
10	dppf	K_2CO_3/*t*-$BuCO_2H$[c]	40	26	>95	41
11	dppm	K_2CO_3	80	36	>95	44
12	dppm	K_2CO_3/*t*-$BuCO_2H$[c]	80	36	>95	-[b]
13	**dppe**	**K_2CO_3**	**80**	**25**	**>95**	**85**
14	dppe	K_2CO_3/*t*-$BuCO_2H$[c]	80	25	>95	-[b]
15	-	*t*-Bu-P_4	80	26	-[b]	-[b]
16	-	*t*-Bu-P_4	60	24	>95	7
17	-	*t*-BuN=$C(NMe_2)_2$	100	7	>95	36
18	dppf	*t*-BuN=$C(NMe_2)_2$	100	4	>95	47

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% **58** or 5 mol% of bidentate $\mathbf{L_2}$ and base (2.5 equiv) in DMA. Conversions were determined by ^{1}H NMR of the crude mixtures. [b] Complex mixture. Yield not determined. [c] 30 mol% of pivalic acid. [d] Not completely pure product.

The cyclization of **87** could be performed using $Pd(OAc)_2$ with K_2CO_3 base, bulky monophosphine **58** and bidentate phosphine ligands at much lower temperatures than previously reported (*Table 14*). As in the previous work,[110] under the reaction conditions, the arylated 8,8'-dihydrobenzo[*e*]-acephenanthrylene spontaneously suffers dehydrogenation to give $C_{20}H_{12}$ aromatic system **95**. In general, the addition of substoichiometric amounts of pivalic acid led to better results when monophosphine **58** was used, but no improvement was observed with bidentate phosphines (*Table 14*, compare for instance entries 3 with 4, and 7 with 8). This

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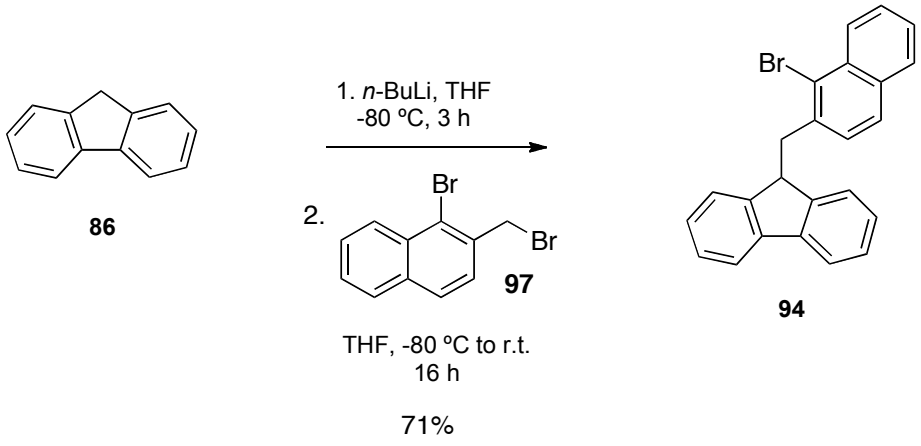
that occurs in the presence of bidentate ligands, potassium carbonate behaves similarly to pivalate anion as an external base, whereas for the intramolecular assisted mechanism, that can occur when monodentate phosphine ligands are employed, chelating pivalate anion is a better base than the corresponding carbonate for this system. The best result for the synthesis of **95** was obtained at 80 ºC in the absence of pivalic acid using K_2CO_3 as the base and dppe as the ligand with an isolated yield of 85% (*Table 14*, entry 13). The use of phosphazene *t*-Bu-P_4 led to complex mixture (*Table 14*, entries 15 and 16), whereas the use of guanidine led to cyclized product in lower yields (*Table 14*, entries 17 and 18).

3.2.2 Bromonaphtyl Fluorene

9-(1-Bromo-2-napthtyl)-9*H*-fluorene (**94**) was prepared following the procedure described for *o*-bromobenzyl analog **87**,[110] by alkylation of the corresponding lithium anion of fluorene **86** with 1-bromo-2-(bromomethyl)naphthalene in 71% yield (*Scheme 44*).



Scheme 44

The direct arylation results are shown in *Table 15*.

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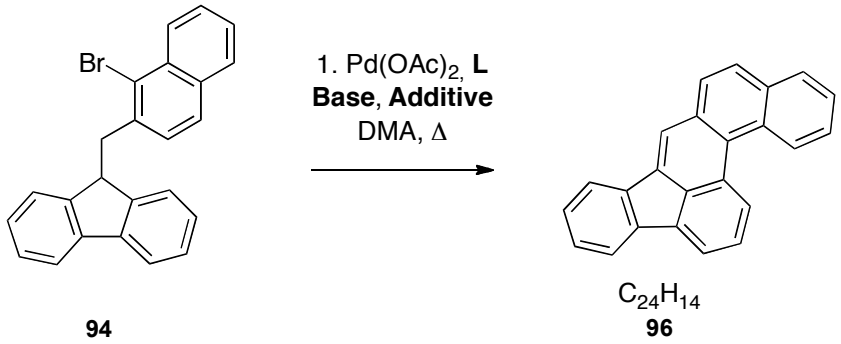
*Table 15: Pd-Catalyzed arylation of bromonaphtyl fluorene **94**.*[a]



94 **96**

Entry	Ligand	Base/Additive	T (°C)	Time (h)	Conversion (%)	Yield (%)
1	**58**	K_2CO_3	100	14	>95	82[b]
2	dppe	K_2CO_3	80	19	>95	39
3	**dppf**	**K_2CO_3/*t*-$BuCO_2H$[c]**	**80**	**19**	**>95**	**79**
4	**Xantphos**	**K_2CO_3**	**80**	**19**	**>95**	**78**

[a] Reactions carried out with 5 mol% $Pd(OAc)_2$, 10 mol% **58** or 5 mol % of bidentate $\mathbf{L_2}$ and base (2.5 equiv) in DMA. Conversions were determined by ^{1}H NMR of the crude mixtures. [b] 95 % pure product determined by ^{1}H NMR. [c] 30 mol% of pivalic acid.

Cyclization of **94** proceeded with concomitant dehydrogenation to afford dibenzo[*e*,*l*]acephenanthrylene **96** in very good yields and relatively mild temperatures with K_2CO_3 and bulky monophosphine **58** or bidentate xantphos, while dppf in the presence of pivalic acid led to similar results (*Table 15*,entries 1, 3 and 4). However, in this particular reaction, when dppe was used as the ligand, poor yield was obtained (*Table 15*,entry 2).

3.2.3 Bromonaphthyl 2,7-Dibromofluorene

A closer model system to study the reaction conditions for the synthesis of crushed fullerene $C_{60}H_{24}$ is compound **98** which presents an additional bromo substituent at C-2 position of the fluorene core. Thus, under palladium-catalyzed cyclization conditions, a stepwise double arylation reaction could take place to form $C_{24}H_{12}$ compound generating first a six and then a five-membered ring (*Scheme 45*).

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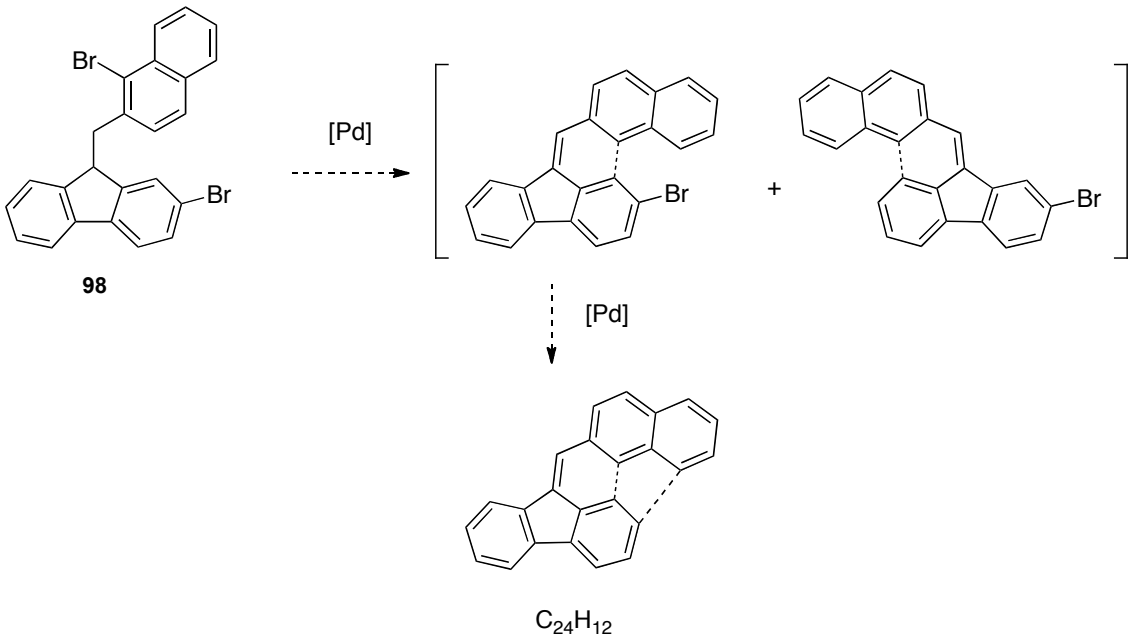
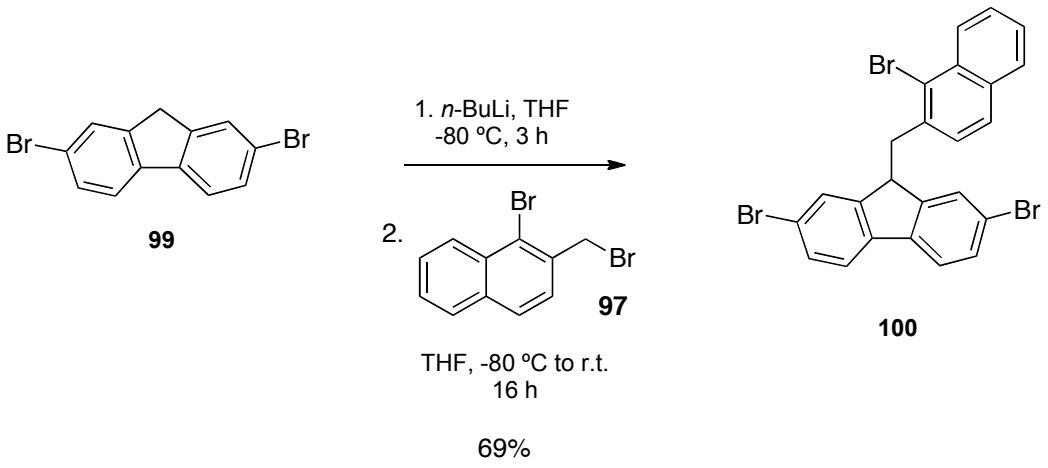


Scheme 45

In this system, the arylation could occur on the unsubstituted aryl ring of the fluorene core, where the second arylation cannot take place (*Scheme 46*). Therefore, we decided to prepare compound **100**, from commercially available 2,7-dibromofluorene **99**, by a deprotonation/alkylation sequence in 69% yield (*Scheme 46*).



Scheme 46

Then we proceed to study the palladium-catalyzed arylation in substrate **100** using some of the best conditions found before as shown in *Table 16*.

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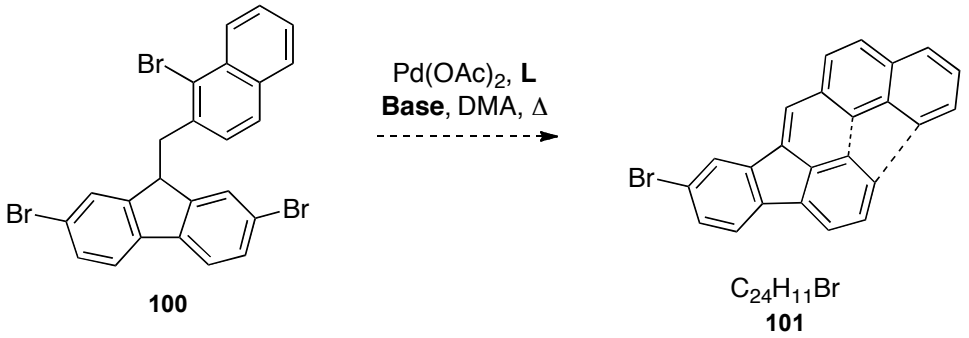
*Table 16: Pd-Catalyzed arylation of 2,7-dibromo-bromonaphthylfluorene **100**.*[a]



100 $C_{24}H_{11}Br$ **101**

Entry	Ligand	Base	T (°C)	Time (h)	Yield (%)
1	Xantphos	K_2CO_3	100	22	-[b]
2	Xantphos	K_2CO_3	80	19	-[b]
3	**58**	K_2CO_3	100	22	-[b]
4	dppe	K_2CO_3	100	14	-[b]
5	dppf	K_2CO_3	100	14	-[b]
6	dppf[c]	K_2CO_3	100	14	-[b]

[a] Reactions carried out with 10 mol% $Pd(OAc)_2$, 20 mol% of **58** or 10 mol% of bidentate $\mathbf{L_2}$ and K_2CO_3 (5 equiv) in DMA. [b] Complex mixture. [c] 20 mol% $Pd(OAc)_2$ and 20 mol% of dppf.

Unfortunately, in this case, all the conditions tried were unsuccessful, even though higher amounts of palladium, ligand, and base were used. Complex mixtures were obtained and no pure compound could be isolated as shown in *Table 16*.

3.2.4 Trisubstituted Truxene Derivatives

Next, we explored the reaction conditions on larger aromatic truxenes systems. Truxenes **22** and **24** bearing three *ortho*-bromophenyl or *ortho*-bromonaphthyl groups, respectively, in a syn fashion were prepared as reported by triple alkylation of trianion of **102** followed by base promoted isomerization (*Scheme 47*).[9]

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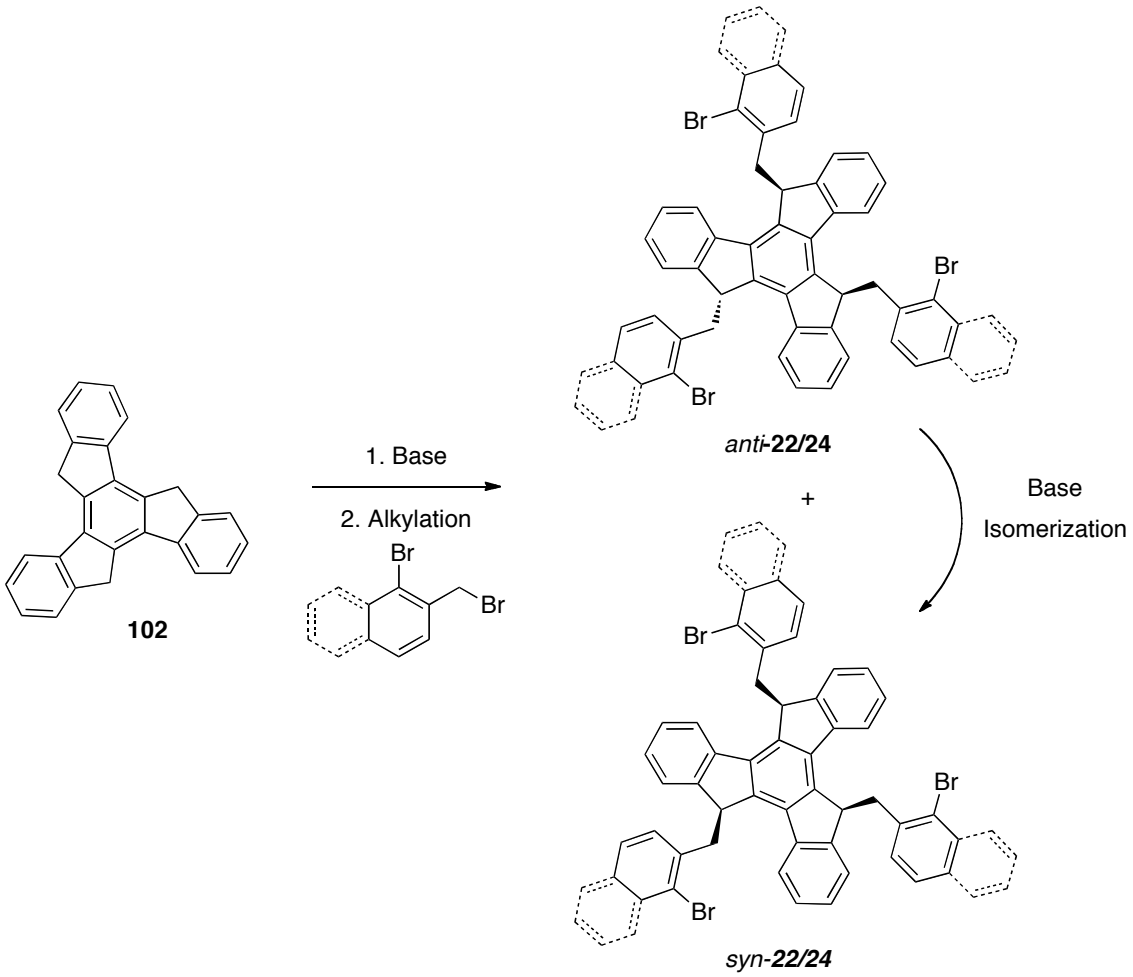

Scheme 47

Originally, **22** with three benzyl groups in a syn relationship, was cyclized at 130 ºC in DMF in good yield (71%), while the cyclization of the *anti*-**22** isomer required higher temperatures (150-165 ºC in DMF or DMA) to give **23** in similar yields (71-79%).[9] Therefore, we prepared exclusively syn isomer of **22**, and essayed our new arylation conditions.

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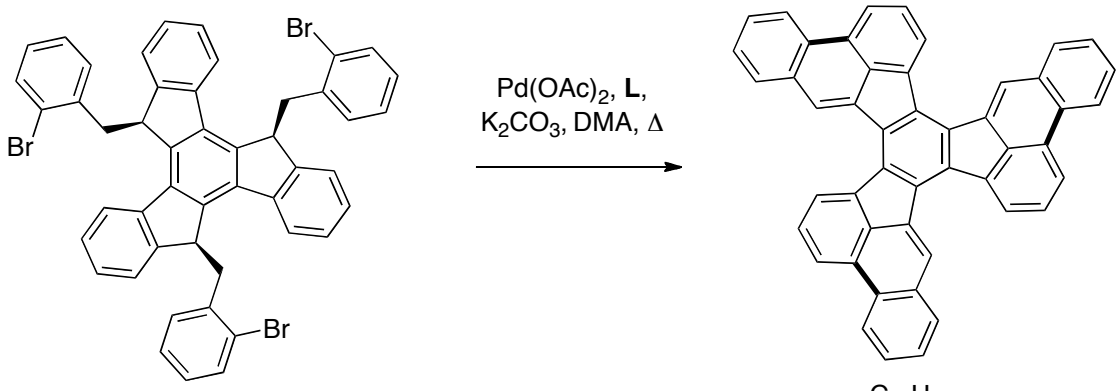
Table 17: Pd-Catalyzed arylation of syn-tribromobenzyl truxene ***22****.*[a]



22 **23**

Entry	Ligand or Additive	T (ºC)	Time (h)	Yield (%)
1	dppf	100	20	-[b]
2	dppe	100	20	-[b]
3	Xantphos	100	20	-[b]
4	Xantphos	120	36	-[b]
5	Xantphos[c]	120	36	11
6	**58**	100	22	-[b]
7	$BnMe_3NBr$[d]	120	36	22

[a] Reactions carried out with 30 mol% $Pd(OAc)_2$, 60 mol% of **58** or 30 mol% of bidentate $\mathbf{L_2}$ and K_2CO_3 (2.5 equiv) in DMA. [b] Complex mixture. Yield not determined. [c] 15 mol% $Pd(OAc)_2$, 15 mol% of ligand. [d] 30 mol% $Pd(OAc)_2$, 100 mol% of $BnMe_3NBr$.

In contrast to our previous results with fluorene model systems, the triple arylation using bulky phosphine or bidentate ligands could not be afforded at milder temperatures than reported. In fact, cyclization of *syn*-derivative 22 at 100 or 120 ºC, usually result in complex mixtures where no pure compound could be isolated (*Table 17*). Poor yields where obtained when Xantphos was added as ligand (*Table 17*, entry 5) or when using simiar conditions as the reported ones[9] (*Table 17*, entry 7). This indicates that triple arylation requires higher temperatures to avoid the formation of mixtures probably coming from the partial dehalogenation of starting

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material and that the best conditions for this particular system still are the reported phosphine-free Jeffery's conditions.[9]

Due to the insolubility of arylated truxenes like compound **22**, a typical purification method for cyclized products was to filter off the precipitated solid and to wash it consecutively with CH_2Cl_2 and acetone. The solid was then suspended in saturated aqueous NaCN solution and stirred for 1 h to remove the rests of palladium catalyst. Finally, the resulting powder was washed again sequentially with water and acetone. Characterization was accomplished by ^{1}H NMR spectroscopy in 1,1,2,2-tetrachloroethane-d_2 at 130 °C and mass spectrometry (MALDI), while ^{13}C spectra could not be obtained, due to the extremely low solubility of compounds **23**/**25** in deuterated solvents.

Next, we proceed to apply our conditions on truxene derivative **24** that will give rise to crushed fullerene, $C_{60}H_{30}$ **25** derivative.[95] As early reported, treatment of **24** with $Pd(OAc)_2$ (10-20 mol%) in the presence of $BnMe_3NBr$ and K_2CO_3 in DMF or DMA at 110-160 ºC gave complex mixtures. However, the use of higher amounts of $Pd(OAc)_2$ (100 mol%, 0.3 equiv per C-C bond formation), 2 equiv of $BnMe_3NBr$ and 10 equiv of K_2CO_3 as the base at 140 ºC for 36 h led to cleaner mixtures and PAH **25** could be isolated in 42% yield. The use of the more soluble Cs_2CO_3 as the base increased the yield of **2** to 53% (80% average per C-C bond formation).[95] The results we obtained for the triple arylation using phosphine ligands are summarized below (*Table 18*).

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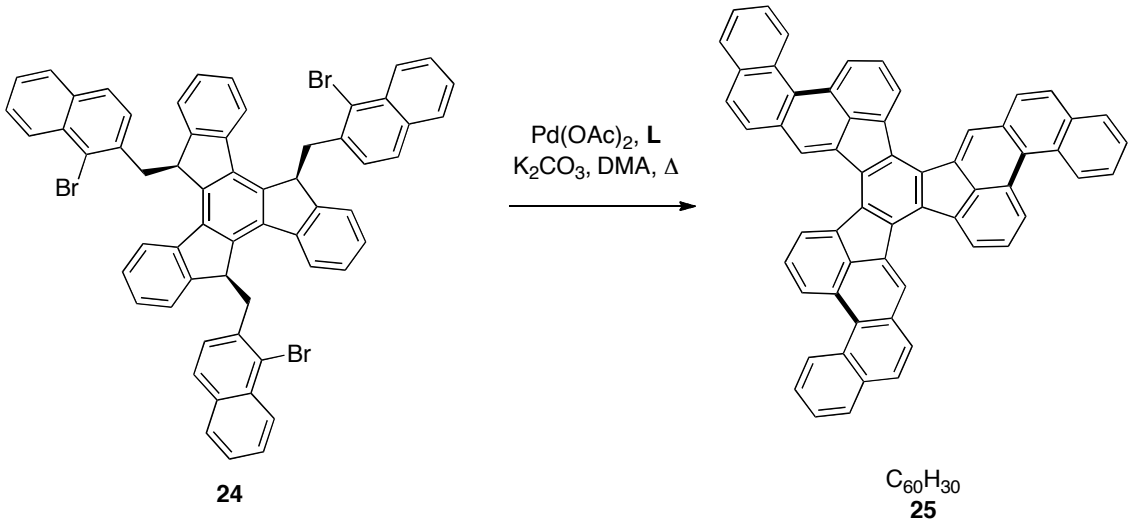
Table 18: Pd-Catalyzed arylation of syn-tribromonaphtyl truxene.[a]



Entry	Ligand	T (°C)	Time (h)	Yield (%)
1	dppf	100	36	-[b]
2	dppf	120	20	27
3	**Xantphos**	**120**	**20**	**61**
4	**58**	**100**	**36**	**59**

[a] Reactions carried out with 30 mol% $Pd(OAc)_2$, 60 mol% of **58** or 30 mol% of bidentate $\mathbf{L_2}$ and K_2CO_3 (2.5 equiv) in DMA. [b] Not complete conversion. Yield not determined.

Triple cyclization of **24** took place in satisfactory yields when bidentate Xantphos or ligand **58** were employed. In these cases, lower amounts of catalyst (30 mol%, 10 mol% per C-C bond formation) and milder temperatures (120 ºC) were required (*Table 18*, entries 3 and 4). The best result was obtained when Xantphos was employed and **25** was isolated in 61% yield, which corresponds to an average of 85% yield per C-C bond formation. The low yields obtained when using dppf ligand could be attributed to the difficulties on isolation and purification of the aromatic hydrocarbon. The same purification and characterization methods earlier employed for $C_{48}H_{24}$ were used for extended $C_{60}H_{30}$ **25**.

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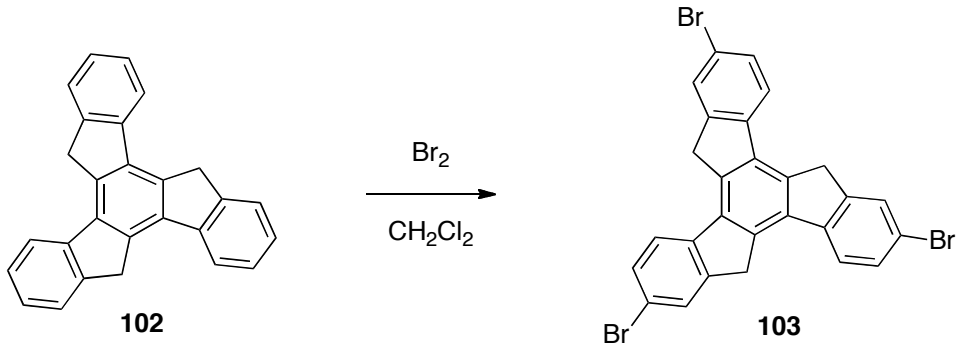
3.2.5 Trisubstituted Tribromotruxene Derivatives

Finally, we proceed to the synthesis of the truxene derivative incorporating six bromo functional groups. This compound could potentially undergo six direct arylation reactions in a single step to furnish $C_{60}H_{24}$ crushed fullerene. Truxene **102**,[9c] was brominated with Br_2, at C-2, C-7, and C-12 positions, as expected from orientation effects in the aromatic electrophilic substitution (*Scheme 48*). The resulting highly insoluble tribromotruxene **103**, was characterized by ^{1}H NMR spectrum in 1,1,2,2-tetrachloroethane-d_2 at 130 °C.



Scheme 48

Triple alkylation of the corresponding trilithium trianion of **103** with 1-bromo-2-(bromomethyl)naphthalene, furnished the desired hexabomotruxene $C_{60}H_{33}Br_6$ **92** (*Scheme 49*). The deprotonation of truxene **103** could be achieved either with NaH in an ultrasound bath or by using *n*-BuLi at low temperatures (-80 ºC). In both cases, trialkylation gave an anti/syn mixture of functionalized truxenes that could not be isomerized to give exclusively the syn isomer in the presence of base. For both methods, when running the reaction at small scales (100 mg, 0.17 mmol of truxene **103**), analytical pure sample of syn product could only be obtained by column chromatography. When the reaction was carried out with NaH in DMF at larger scales and lower concentrations, syn product slowly precipitate from the reaction mixture and could be filtered off, washed and isolated in 19% pure yield. Again ^{1}H NMR spectrum had to be measured at 130 °C in 1,1,2,2-tetrachloroethane-d_2, while MALDI mass spectrometry only showed dehalogenation and fragmentation peaks.

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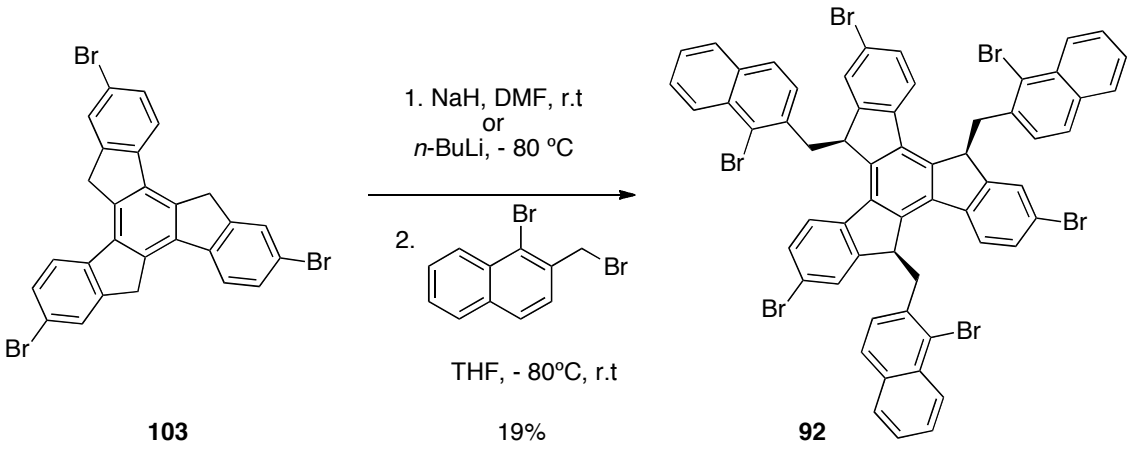

103 **92**

Scheme 49

Hexabromotruxene **92** was submitted to palladium-catalyzed direct arylation. Under all the reaction conditions employed, arylation of **92** followed by preliminary washings, furnished in a brownish/black insoluble solid. Due to the even higher insolubility of the resulting mixture, these could not be analyzed by high temperature NMR, and only be examined by means of mass spectrometry MALDI and LDI experiments. As a result of the difficulties and high effort required for the separation and complete purification of the product from the crude mixtures (see experimental section), we decided to initially screen different conditions and find the most suitable ones according to preliminary MALDI-TOF$^+$ analysis. When $Pd(OAc)_2$, Xantphos, and K_2CO_3 were used under different conditions in DMA, only complex mixtures of compounds were detected and no clear peak corresponding to $C_{60}H_{24}$ (**93**) was found. Changing the ligand to dppp, **58**, or using $BnMe_3NBr$ did not give better result. Finally, using dppe as ligand showed clear evidences for the formation of $C_{60}H_{24}$ (**93**). The best results were obtained using 2 equiv of $Pd(OAc)_2$ and dppe, 15 equiv of K_2CO_3 in DMA at 140 ºC for 36 h (*Scheme 50*).

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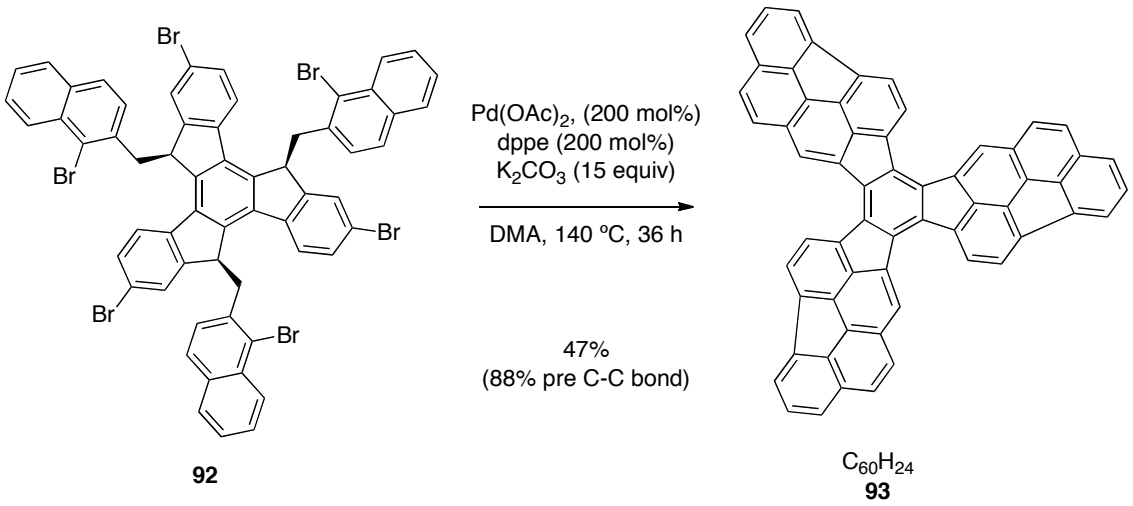

Scheme 50

After further purification by washing with organic solvents, MALDI-TOF$^+$ experiment of the isolated orange solid showed a single peak at *m/z* 744.3. This peak corresponds to $C_{60}H_{24}$, and presents an experimental isotopic pattern in agreement with the theoretical calculated one for this molecule (*Figure 21*). The molecular mass of the purified compound reflects that the unprecedented six-fold arylation takes place in a significant 47% yield, which means an 88% average per C-C bond formation and additional in situ dehydrogenation.

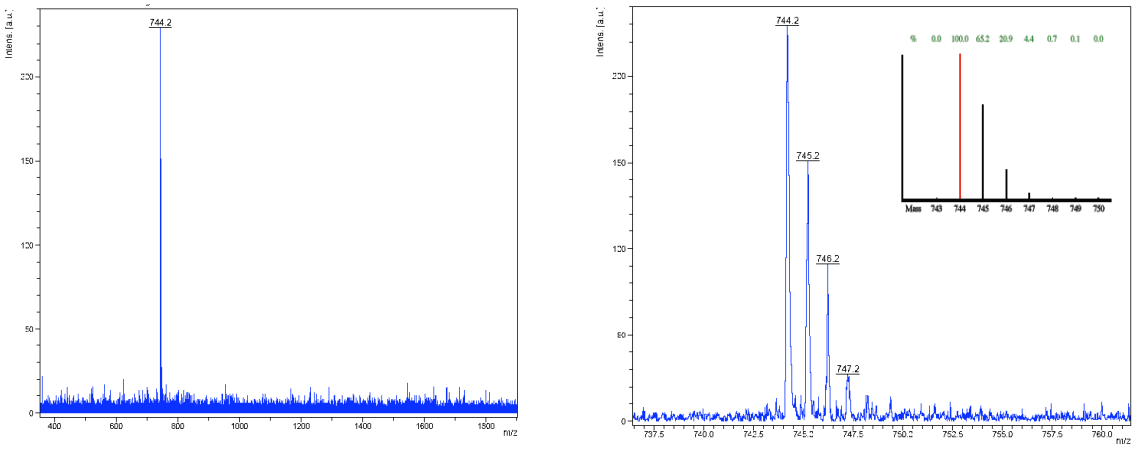

*Figure 21: MALDI-TOF$^+$ (dithranol-THF-Ag) spectra of **93**, $C_{60}H_{30}$ (right) and zoomed region at m/z 744 showing the isotopic experimental pattern in agreement with the theoretical calculated one (left).*

The reaction was reproduced twice under these conditions and MALDI-TOF$^+$ analysis showed again a sole peak corresponding to $C_{60}H_{24}$. When the compound

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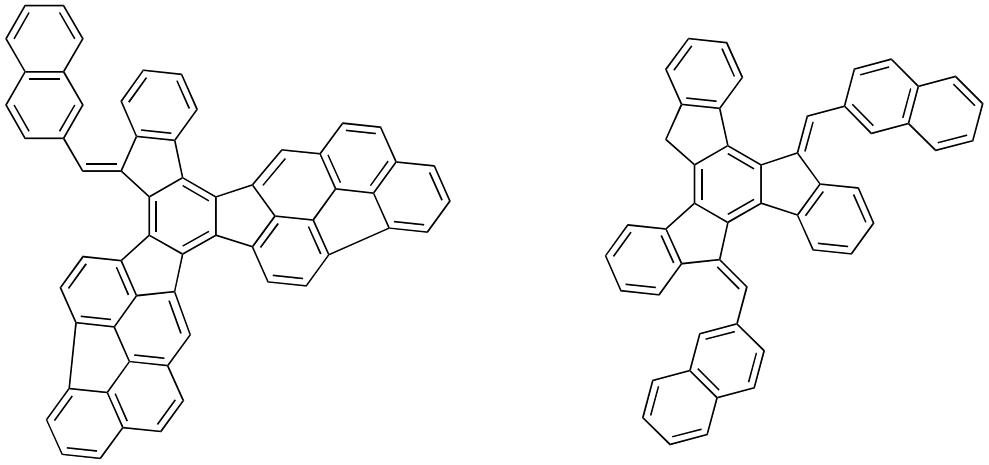
was not completely purified, on the negative ionization detection mode, two peaks at *m*/*z* 748 and 618 were also detected. Peak at *m*/*z* 748 could be attribute to $C_{60}H_{28}$ (**104**) corresponding to the tetraarylation of starting material and double debromination reaction, whereas the peak at *m*/*z* 618 was attributed to the lost of bromines and a bromonaphtyl branch (**105**) (*Figure 22*). Additional purification by washings with organic solvents of the resulting solid, lead again to a sole peak detected for MALDI positive ionization method corresponding to $C_{60}H_{24}$ while no peaks were detected in the negative mode. Due to the insolubility of the compound, suitable crystals for X-Ray diffraction could not be obtained.



Chemical Formula: $C_{60}H_{28}$
Exact Mass: 748.22

Chemical Formula: $C_{49}H_{30}$
Exact Mass: 618.23

Figure 22: Possible by products on the palladium-catalyzed hexaarylation reaction of $C_{60}H_{33}Br_6$.

As it has been previously shown for $C_{60}H_{30}$ molecule,[95b,98] increasing the incident laser upon $C_{60}H_{24}$ was increased up to 80% (*ca* 8x) on MALDI-TOF$^+$ experiment, cyclodehydrogenation took place and a peak at *m*/*z* 720.1 with the corresponding isotopic pattern of closed fullerene C_{60} was obtained (*Figure 23*).

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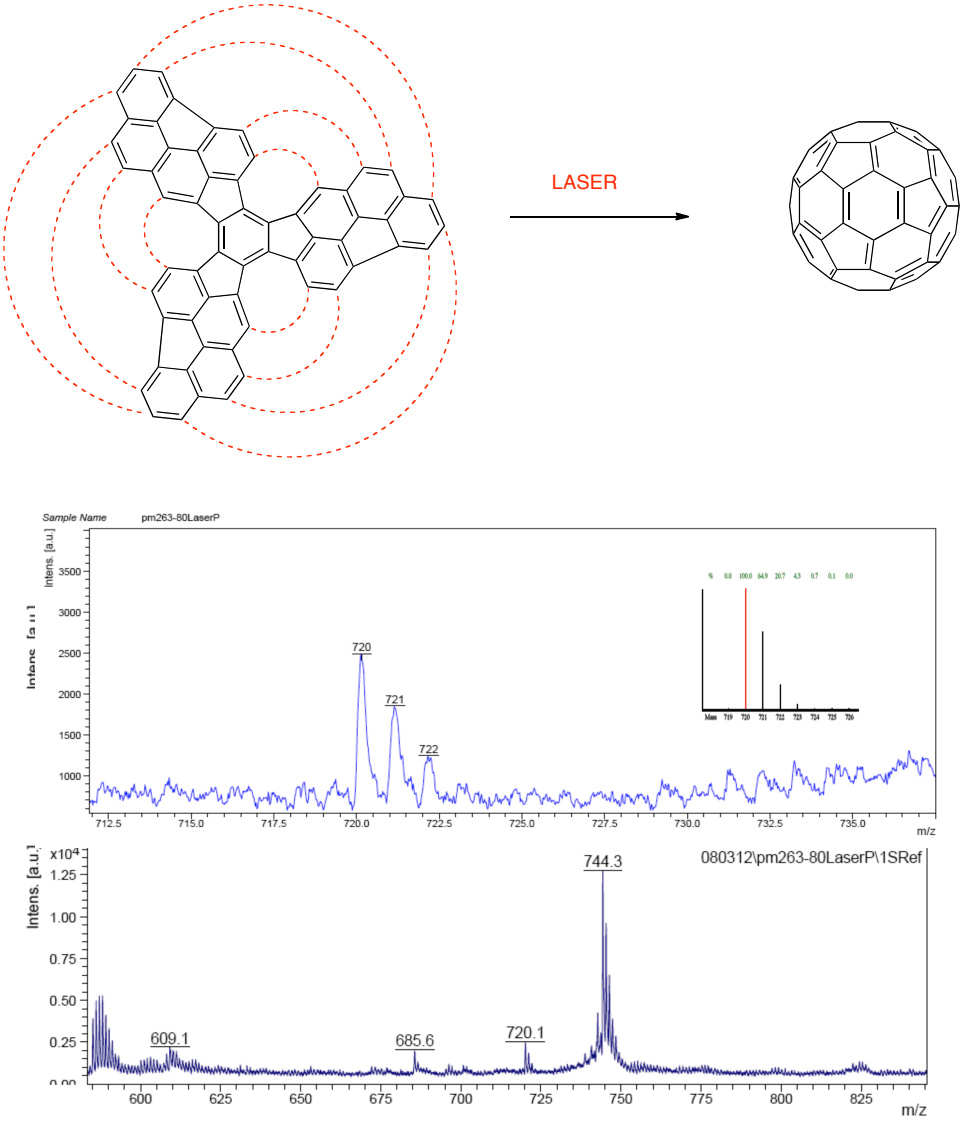

Figure 23: MALDI-TOF$^+$(dithranol-THF-Ag) spectra of $C_{60}H_{24}$ (bottom) that upon increasing laser irradiation present a peak at m/z 720 corresponding to C_{60}. The zoom region at m/z 720 shows that the isotopic experimental pattern of C_{60} is in agreement with the theoretical calculated one (above).

Recently, fullerene C_{60} and azafullererene $C_{57}N_3$ have been formed from $C_{60}H_{30}$ or $C_{57}H_{33}N_3$ precursors via a platinum-surface-catalyzed cyclodehydrogenation process.[138] STM images were obtained for the deposited triangular fullerene precursors that, after annealing to 750 K, formed round-shaped C_{60} fullerene,

138 Otero, G.; Biddau, G.; Sánchez-Sánchez, C.; Caillard, R.; López, M. L.; Rogero, C.; Palomares, F. G.; Cabello, N.; Basanta, M. A.; Ortega, J.; Méndez, J.; Echavarren, A. M.; Pérez, R.; Gómez-Lor, B.; Martín-Gago, J. M. *Nature* **2008**, *454*, 865-868.

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indistinguishable from those images of authentic fullerene C_{60}, and ball shape of the previously unknown heterofullerene $C_{57}N_3$ as shown in *Figure 24*.[138]

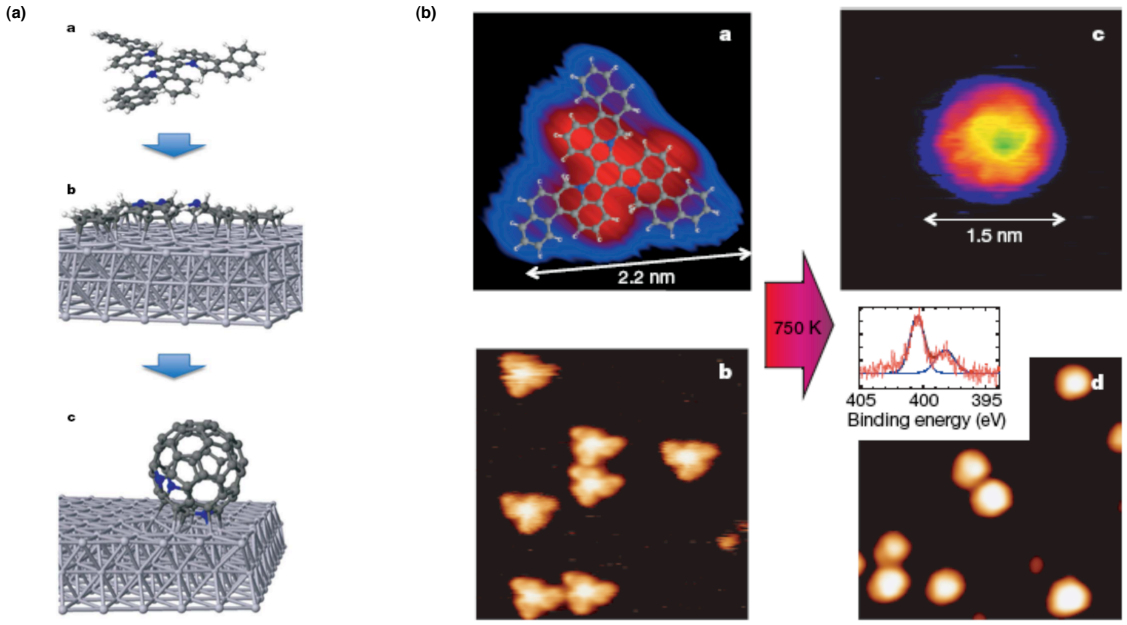

Figure 24: (a) Optimized geometrical structure of $C_{57}H_{33}N_3$ and $C_{57}N_3$, and (b) STM images of the surface-catalyzed cyclodehydrogenations process.

Currently, $C_{60}H_{24}$ is being studied in surface depositions and submitted to platinum-surface-catalyzed cyclization/degydrogenation reaction for the preparation of C_{60}.

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4.Conclusions

Palladium-catalyzed direct arylation reactions via C-H bond functionalization represent an attractive alternative to traditional cross-coupling reactions with organometallic reagents.

By combining experimental and theoretical results, we have contributed to the elucidation of the mechanism that proceeds in the intramolecular palladium-catalyzed direct arylation that have given rise to a change of paradigm compared to the previously favored S_EAr mechanism. According to our results, a base-assisted proton abstraction mechanism as the overall rate-determining step has been established.

We have optimized the reaction to obtain milder and more efficient conditions for the synthesis of polyaromatic systems. We have showed that, in many cases, the use of bidentate phosphines enhances the reactivity of the intramolecular direct arylation. According to experimental and theoretical studies, when bidentate phosphines are employed the mechanism proceeds more likely through an intermolecular base-assisted proton abstraction mechanism.

Finally, applying our optimized reaction conditions, we have prepared a series of polyaromatic hydrocarbons related to fullerene subunits culminating in the preparation of $C_{60}H_{24}$ via an unprecedented six-fold cyclization reaction, that until now is the highest number of subsequent direct arylations in one single step. By applying high laser irradiation to $C_{60}H_{24}$ (MALDI-TOF experiments), we could form C_{60} fullerene as one of the rare examples for the designed synthesis of fullerenes. This three-branched polyaromatic crushed fullerene is a highly attractive candidate for material applications.

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Experimental Section

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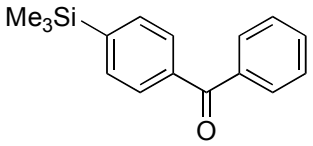
Methods

All reactions were carried out under N_2 or Ar. Solvents were dried using a Solvent Purification System (SPS) or using standard procedures,[139] except for dimethylacetamide that was purchased anhydrous and packaged under N_2 (Aldrich). Analytical thin layer chromatography was carried out using TLC-aluminium sheets with 0.2 mm of silica gel (Merk GF_{234}). Flash chromatography purifications were carried out using flash grade Silica gel (SDS Chromatogel 60 ACC, 40-60 μm), Florisil (SDS, 60-100 mesh) or Alumina neutre (SDS, 0.063-0.2 mm, pH 6.3-7.7). NMR spectra (δ given in ppm) were recorded at 23 ºC on a Bruker Avance 400 Ultrashield (400 MHz for ^1H, and 100 MHz for ^{13}C) and at 130 ºC on a Bruker Avance 500 Ultrashield (500 MHz for ^1H) spectrometers at the *Institut Català d'Investigaciò Química (ICIQ)*. Mass spectra were recorded on a Waters Micromass LCT Premier (ESI) and Waters Micromass GCT (EI, CI) and Bruker Daltonics Autoflex (MALDI, LDI) spectrometers at the *ICIQ*. Melting points were determined using a Büchi melting point apparatus.

3.1 Mechanistic and Optimization Studies

Synthesis of benzophenones 60j and 60k

4-(Trimethylsilyl)benzophenone (60j)



General procedure for the synthesis of substituted benzophenones: [140] In a two neck flask a mixture of 4-trimethylsilylphenylboronic acid (498 mg, 2.57 mmol) and Cs_2CO_3 (4.19 g, 13.0 mmol) in anhydrous toluene (30 mL), $Pd(PPh_3)_4$ (42 mg, 0.12 mmol) was added followed by benzoyl chloride (728 mg, 5.16 mmol). The reaction mixture was heated at 100 ºC for 16 h. The solution was diluted with

139 (a) Burfield, D. R.; Lee, K.-H.; Smithers, R. H. *J. Org. Chem.* **1977**, *42*, 3060-3065. (b) Burfield, D. R.; Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 3966-3968. (c) Perrin, D. D.; Armarego, S. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon: New York, **1980**.

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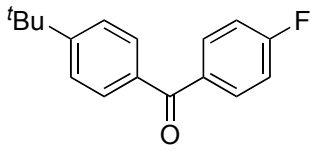
EtOAc (50 mL) and washed successively with water (70 mL), sat. solution of $NaHCO_3$ (70 mL) and sat. solution of NaCl (70 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, 5 to 10% EtOAc/hexane) to give **60j** (497 mg, 76%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.81 (m, 2H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.59 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.50-7.46 (m, 2H), 0.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.73, 146.18, 137.65, 137.57, 133.10, 132.30, 129.99, 128.94, 128.18, -1.35. HRMS-CI *m/z* calcd for $C_{16}H_{19}OSi$ $[M+H]^+$ 255.1211, found 255.1205.

4-*tert*-Butyl-4'-fluorobenzophenone (60k)



The general procedure for the synthesis of substituted benzophenones was followed: 4-tert-butylphenylboronic acid (503 mg, 2.81 mmol), Cs_2CO_3 (4.59 g, 14.1 mmol), toluene (30 mL), $Pd(PPh_3)_4$ (16 mg, 0.14 mmol), 4-fluorobenzoyl chloride (890 mg, 5.62 mmol), EtOAc (50 mL), water (70 mL), $NaHCO_3$ (70 mL), NaCl (70 mL). The residue was chromatographed (SiO_2, 2 to 10% EtOAc/hexane) to give **60k** (670 mg, 90%) as a white solid: mp 74-75 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (m, 2H), 7.73 (dt, *J* = 8.6, 2.0 Hz, 2H), 7.50 (dt, *J* = 8.6, 2.0 Hz, 2H), 7.16 (tt, *J* = 8.8, 2.6 Hz, 2H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.01, 165.26 (d, *J* = 253.4 Hz), 156.29, 134.72, 134.11 (d, *J* = 3.3 Hz) 132.55 (d, *J* = 9.3 Hz), 129.96, 125.32, 115.35 (d, *J* = 21.3 Hz), 35.12, 31.13. HRMS-CI *m/z* calcd for $C_{17}H_{17}OF$ $[M]^+$ 256.1263, found 256.1269.

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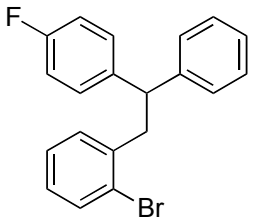
Synthesis of 55f-k

1-Bromo-2-(2-(4-fluorophenyl)-2-phenylethyl)benzene (55f)



General procedure for the synthesis of 55: The yield was not optimized. In a two neck flask equipped with a condenser 1,2-dibromoethane (50 μL, 0.66 mmol) was added over a suspension of 2-bromobenzylbromide (1.98 g, 7.92 mmol) and Mg (1.35 g, 55.4 mmol) in anhydrous Et_2O (25 mL). The exothermic reaction was stirred for 5 h under reflux. Then the reaction mixture was cooled to room temperature and the supernatant was added dropwise, using an additional funnel, over a solution of 4-fluorobenzophenone (931 mg, 4.65 mmol) in anhydrous Et_2O (25 mL). Once the addition was completed the reaction mixture was stirred at 23 ºC overnight and then water was added (30 mL) and the product was extracted with Et_2O (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated to give the crude alcohol that was used without further purification in the next step. Triethylsilane (4.04 mL, 23.2 mmol) and $BF_3{\cdot}OEt_2$ (1.93 mL, 13.9 mmol) were added to a solution of the previous alcohol in anhydrous CH_2Cl_2 (25 mL) at 0 ºC and the reaction mixture was stirred at this temperature for 1 h. A sat. solution of NH_4Cl (30 mL) was added and the product was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, hexane) to give **55f** (853 mg, 51%, for the two steps) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.49 (m, 1H), 7.27-7.11 (m, 6H), 7.01-6.95 (m, 2H), 6.92 (tt, J = 8.7, 2.0 Hz, 2H) 6.75-6.72 (m, 2H), 4.38 (t, J = 7.8 Hz, 1H), 3.45 (dd, J = 13.6, 7.4 Hz, 1H), 3.40 (dd, J = 13.6, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.39 (d, J = 244.1 Hz), 143.76, 139.61 (d, J = 3.4 Hz), 139.90, 132.71, 131.42, 129.56 (d, J = 7.6 Hz), 128.40, 128.00, 127.77, 126.89, 126.42, 124.75, 115.06 (d, J = 21.2 Hz), 49.88, 42.39. HRMS-CI *m/z* calcd for $C_{20}H_{15}BrF$ $[M-H]^+$ 353.0341, found. 353.0338.

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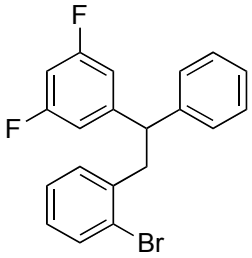
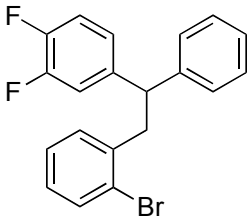
1-Bromo-2-(2-(3,5-difluorophenyl)-2-phenylethyl)benzene (55g)



The general procedure for the synthesis of **55** was followed: 1,2-dibromoethane (25 μL, 0.33 mmol), 2-bromobenzylbromide (990 mg, 3.96 mmol), Mg (674 mg, 27.7 mmol), Et_2O (solvent, 2 x 15 mL), 3,5-difluorobenzophenone (502 mg, 2.31 mmol), water (for the first extraction 20 mL), Et_2O (for the first extraction 3 x 25 mL), triethylsilane (3.06 mL, 19.2 mmol), $BF_3{\cdot}OEt_2$ (1.46 mL, 11.6 mmol), CH_2Cl_2 (solvent, 25 mL), NH_4Cl (for the second extraction, 30 mL), CH_2Cl_2 (for the second extraction, 3 x 40 mL). The residue was chromatographed (SiO_2, hexane) to give **55g** (273 mg, 32% for the two steps) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.51 (m, 1H), 7.30-7.18 (m, 5H), 7.04-6.98 (m, 2H), 6.78-6.75 (m, 1H), 6.74-670 (m, 2H), 6.61 (tt, J = 8.9, 2.3 Hz, 1H), 4.37 (t, J = 7.7 Hz, 1H), 3.42 (d, J = 7.8, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.90 (dd, J = 248.0, 13.0 Hz), 148.02 (t, J = 8.3 Hz), 142.48, 138.42, 132.84, 131.35, 128.58, 128.03, 128.00, 127.03, 126.85, 124.67, 111.02 (dd, J = 18.4, 6.6 Hz), 101.80 (t, J = 25.3 Hz), 50.41, 41.94. HRMS-CI *m/z* calcd for $C_{20}H_{15}BrF_2$ $[M]^+$ 372.0325, found 372.0316.

1-Bromo-2-(2-(3,4-difluorophenyl)-2-phenylethyl)benzene (55h)



The general procedure for the synthesis of **55** was followed: 1,2-dibromoethane (50 μL, 0.66 mmol), 2-bromobenzylbromide (2.01 g, 7.92 mmol), Mg (1.31 g, 55.4 mmol), Et_2O (solvent, 2 x 15 mL), 3,4-difluorobenzophenone (1.04 g,

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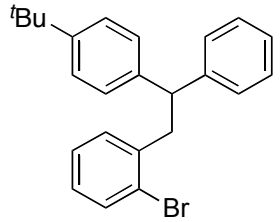
3 x 25 mL), triethylsilane (6.20 mL, 38.4 mmol), $BF_3{\cdot}OEt_2$ (2.90 mL, 23.1 mmol), CH_2Cl_2 (solvent, 25 mL), NH_4Cl (for the second extraction, 30 mL), CH_2Cl_2 (for the second extraction, 3 x 40 mL). The residue was chromatographed (SiO_2, hexane) to give **55h** (716 mg, 42% for the two steps) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.49 (m, 1H), 7.29-7.25 (m, 2H), 7.21-7.17 (m, 3H), 7.02-6.95 (m, 4H), 6.88-6.84 (m, 1H), 6.75-6.73 (m, 1H), 4.35 (t, *J* = 7.7 Hz, 1H), 3.43 (dd, *J* = 7.6, 13.7 Hz, 1H), 3.38 (dd, *J* = 8.2, 13.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.10 (dd, *J* = 247.6, 12.4 Hz), 148.88 (dd, *J* = 246.8, 12.2 Hz), 143.02, 141.00 (t, *J* = 4.4 Hz), 138.61, 132.80, 131.37, 128.54, 127.94, 126.99, 126.70, 124.69, 123.99 (dd, *J* = 5.9, 3.7 Hz), 116.90 (dd, *J* = 17.2, 6.1 Hz), 49.88, 42.20. HRMS-CI *m/z* calcd for $C_{26}H_{15}BrF_2$ $[M]^+$ 372.0325, found. 372.0311.

1-Bromo-2-(2-(4-*tert*-butylphenyl)-2-phenylethyl)benzene (55i)



The general procedure for the synthesis of **55** was followed: 1,2-dibromoethane (20 µL, 0.26 mmol), 2-bromobenzylbromide (721 mg, 2.88 mmol), Mg (464 mg, 19.1 mmol), Et_2O (solvent, 2 x 10 mL), 4-*tert*-butylbenzophenone (400 mg, 1.68 mmol), water (for the first extraction 15 mL), Et_2O (for the first extraction 3 x 20 mL), triethylsilane (2.30 mL, 14.4 mmol), $BF_3{\cdot}OEt_2$ (1.08 mL, 8.52 mmol), CH_2Cl_2 (solvent, 25 mL), NH_4Cl (for the second extraction, 30 mL), CH_2Cl_2 (for the second extraction, 3 x 40 mL). The residue was chromatographed (SiO_2, hexane) to give **55i** (424 mg, 67%, for the two steps) as a white solid mp 52-54 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.49 (m, 1H), 7.28-7.14 (m, 9H), 6.98-6.96 (m, 2H), 6.77-6.75 (m, 1H), 4.36 (t, *J* = 7.76 Hz, 1H), 3.48 (dd, *J* = 13.68, 6.98 Hz, 1H), 3.42 (dd, *J* = 13.68, 8.56 Hz, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.98, 143.99, 141.01, 139.41, 132.61, 131.43, 128.26, 128.24, 127.59, 126.78, 126.18, 125.20, 124.81, 50.21, 42.34, 34.33, 31.36. HRMS-CI *m/z* calcd for $C_{24}H_{24}Br$ $[M-H]^+$ 391.1067, found 391.1061

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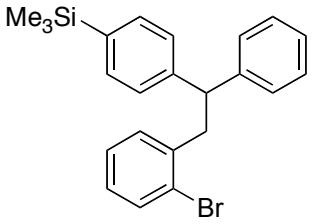
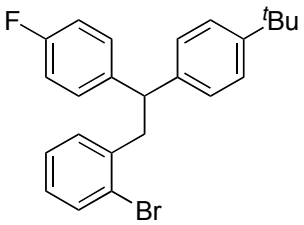
1-Bromo-2-(2-(4-(trimethylsilyl)phenyl)-2-phenylethyl)benzene (55j)



The general procedure for the synthesis of **55** was followed: 1,2-dibromoethane (14 μL, 0.18 mmol), 2-bromobenzylbromide (541 mg, 2.16 mmol), Mg (352 mg, 14.4 mmol), Et_2O (solvent, 2 x 10 mL), 4-(trimethylsilyl)benzophenone **60j** (300 mg, 1.18 mmol), water (for the first extraction 15 mL), Et_2O (for the first extraction 3 x 20 mL), triethylsilane (1.00 mL, 6.27 mmol), $BF_3{\cdot}OEt_2$ (0.48 mL, 3.79 mmol), CH_2Cl_2 (solvent, 25 mL), NH_4Cl sat. solution (for the second extraction, 3 x 30 mL), CH_2Cl_2 (for the second extraction, 3 x 40 mL). The residue was chromatographed (SiO_2, hexane) to give **55j** (221 mg, 46% for the two steps) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.49 (m, 1H), 7.41 (d, J = 7.9 Hz, 2H) 7.24-7.14 (m, 7H), 6.98-6.96 (m, 2H), 6.78-6.75 (m, 1H), 4.38 (t, J = 7.6 Hz, 1H), 3.52-3.41 (m, 2H), 0.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.66, 143.75, 139.28, 138.01, 133.45, 132.68, 131.43, 128.31, 128.26, 127.66, 127.43, 126.84, 126.29, 124.84, 50.68, 42.17, -1.08. HRMS-CI *m/z* calcd for $C_{23}H_{25}SiBr$ $[M]^+$ 408.0909, found 408.0910.

1-Bromo-2-(2-(4-*tert*-butylphenyl)-2-(4'-fluorophenylethyl)benzene (55k)



The general procedure for the synthesis of **55** was followed: 1,2-dibromoethane (18 μL, 0.23 mmol), 2-bromobenzylbromide (703 mg, 2.81 mmol), Mg (486 mg, 20.0 mmol), Et_2O (solvent, 2 x 10 mL), 4-*tert*-butyl-4'-fluorobenzophenone **60k** (402 mg, 1.57 mmol), water (for the first extraction 15 mL), Et_2O (for the first

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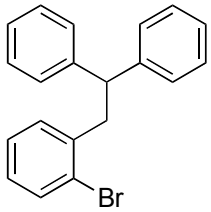
7.99 mmol), CH_2Cl_2 (solvent, 25 mL), sat. solution NH_4Cl (for the second extraction, 30 mL), CH_2Cl_2 (for the second extraction, 3 x 30 mL). The residue was chromatographed (SiO_2, hexane) to give **55k** (382 mg, 59% for the two steps) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.48 (m, 1H), 7.29 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 7.12-7.10 (m, 2H), 6.99-6.96 (m, 2H), 6.89 (tt, *J* = 8.7, 2.0 Hz, 2H), 6.75-6.73 (m, 1H), 4.35 (dd, *J* = 8.8, 6.7 Hz, 1H), 3.47 (dd, *J* = 13.5, 6.5 Hz, 1H), 3.36 (dd, *J* = 13.5, 8.9 Hz, 1H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.35 (d, *J* = 243.9 Hz), 149.18, 140.82, 139.67 (d, *J* = 3.7 Hz), 139.17, 132.68, 131.44, 129.66 (d, *J* = 7.3 Hz), 127.71, 127.47, 126.86, 125.29, 124.77, 114.99 (d, *J* = 21.2 Hz), 49.46, 42.48, 34.36, 31.35. HRMS-CI *m/z* calcd for $C_{24}H_{23}BrF$ $[M-H]^+$ 409.0967, found 409.0983.

(2-(2-Bromophenyl)ethane-1,1-diyl)dibenzene 55l



The general procedure for the synthesis of **55** was followed: 1,2-dibromoethane (0.13 mL, 1.49 mmol), 2-bromobenzylbromide (4.48 g, 17.9 mmol), Mg (3.05 g, 125 mmol), Et_2O (solvent, 2 x 60 mL), benzophenone **60l** (1.92 g, 10.5 mmol), water (for the first extraction 150 mL), Et_2O (for the first extraction 3 x 150 mL), triethylsilane (5.97 mL, 37.0 mmol), $BF_3{\cdot}Et_2O$ (2.82 mL, 22.3 mmol), CH_2Cl_2 (solvent, 40 mL), sat. solution NH_4Cl (for the second extraction, 100 mL), CH_2Cl_2 (for the second extraction, 3 x 100 mL). The residue was chromatographed (SiO_2, hexane) to give **55l** (1,12 g, 75% for the two steps) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 77.49-7.52 (m, 1H), 7.20-7.27 (m, 11H), 7.14-7.18 (m, 1H), 6.95-7.00 (m, 1H), 6.74-6.77 (m, 1H), 4.39 (t, *J* = 7.8 Hz, 1H), 3.46 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 139.2, 132.7, 131.4, 128.3, 128.1, 127.7, 126.8, 126.3, 124.8, 50.6, 42.2.

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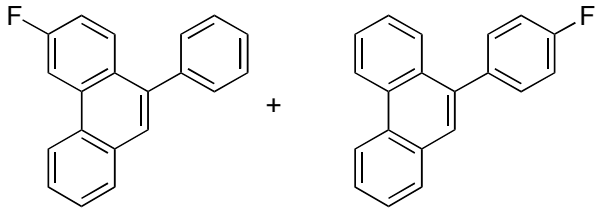
Synthesis of phenanthrenes 56f-k and 57f-k

3-Fluoro-10-phenylphenanthrene (56f)

9-(4-Fluorophenyl)phenanthrene (57f)



56f **57f**

General procedure for the intramolecular arylation reaction: A solution of the bromoarene **55f** (104 mg, 0.295 mmol), $Pd(OAc)_2$ (3.3 mg, 0.015 mmol), 2-(diphenylphosphino)-2'-(*N,N*-dimethylamino)biphenyl (**58**) (11.8 mg, 0.071 mmol) and K_2CO_3 (89.9 mg, 0.650 mmol) in anhydrous DMA (1.2 mL), was heated in a vial at 135 ºC for 16 h. The reaction mixture was cooled to room temperature, filtered through Celite and rinsed with EtOAc. A sat. solution of NaCl was added (5 mL) and it was extracted with EtOAc (3 x 7 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was treated with DDQ.

General procedure for the aromatization: A solution of the above crude product and DDQ (201 mg, 0.885 mmol) in toluene (5 mL) was refluxed 16 h. The reaction mixture was cooled to room temperature, filtered through Celite and rinsed with CH_2Cl_2. The solvent was evaporated and the residue was chromatographed (SiO_2, 2 to 6% CH_2Cl_2/hexane) to give a 1.6:1 mixture of regioisomers **56f/57f** (58 mg, 72%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 8.3 Hz, 1H **57f**), 8.72 (d, *J* = 8.3 Hz, 1H **57f**), 8.58 (d, *J* = 8.4 Hz, 1H **56f**), 8.37 (dd, *J* = 11.0, 2.7 Hz, 1H **56f**), 7.91-7.87 (m, 2H **56f** + 1H **57f**), 7.85 (d, *J* = 8.1 Hz, 1H **57f**), 7.69-7.60 (m 3H **56f** + 4H **57f**) 7.56-7.44 (m 5H **56f** + 3H **57f**), 7.29-7.25 (m, 1H **56f**), 7.20 (tt, *J* = 8.6, 2.0 Hz, 2H **57f**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.32 (d, *J* = 246.2 Hz) **57f**, 161.48 (d, *J* = 246.0 Hz) **56f**, 140.54 **56f**, 138.44 **56f**, 137.68 **57f**, 136.67 (d, *J* = 3.4 Hz) **57f**, 132.38 (d, *J* = 8.1 Hz) **56f**, 131.95 **56f**, 131.59 (d, *J* = 8.0 Hz) **57f**, 131.44 **57f**, 131.09 **57f**, 130.63 **57f**, 129.98 **57f**, 129.96 **56f**, 129.37 **56f**, 129.33 **56f**,

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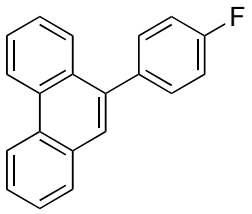
J = 1.5 Hz) **56f**, 127.66 **57f**, 127.52 **56f**, 127.45 **56f**, 126.92 **57f**, 126.70 **57f**, 126.69 **56f**, 126.68 **57f**, 126.61 **56f**, 126.59 **57f**, 126.53 **57f**, 122.96 **57f**, 122.74 **56f**, 122.54 **57f**, 115.32 (d, *J* = 23.4 Hz) **56f**, 115.23 (d, *J* = 21.3 Hz) **57f**, 107.93 (d, *J* = 22.0 Hz) **56f**. HRMS-CI *m/z* calcd for $C_{20}H_{13}F$ $[M]^+$ 272.1001, found 272.0995.

9-(4-Fluorophenyl)phenanthrene (57f)



General procedure for the Suzuki coupling:[141] The yield was not optimized. A solution of 9-bromophenantrene (199 mg, 0.745 mmol), KF (129 mg, 2.23 mmol), $Pd_2(dba)_3$ (39.2 mg, 0.102 mmol), 2-(dicyclohexylphosphino)biphenyl (29.7 mg, 0.005 mmol) and 4-fluorophenylboronic acid (127 mg, 0.908 mmol) in anhydrous toluene (5 mL) was heated under reflux overnight. The reaction was cooled to room temperature, a sat. solution of NaCl (15 mL) was added and the product was extracted with Et_2O (3 x 30 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, hexane) to give **57f** (88 mg, 44%) as a white solid: mp 148-150 ºC (lit[141] mp 148-149 ºC). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (d, *J* = 8.5 Hz, 1H), 8.72 (d, *J* = 8.6 Hz, 1H), 7.90-7.84 (m, 2H), 7.70-7.60 (m, 4H), 7.56-7.48 (m, 3H), 7.21 (tt, *J* = 8.8, 2.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.33 (d, *J* = 246.3 Hz), 137.68, 136.69 (d, *J* = 3.4 Hz), 131.59 (d, *J* = 7.3 Hz), 131.44, 131.10, 130.64, 129.99, 128.63, 127.66, 126.92, 126.70, 126.68, 126.59, 126.53, 122.96, 122.54, 115.23 (d, *J* = 21.2 Hz).

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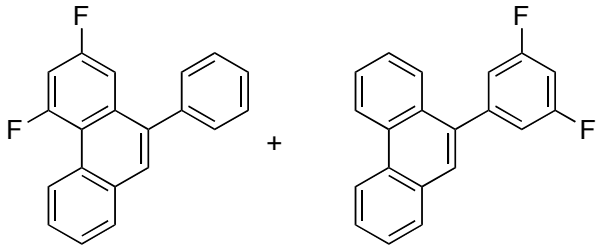
2,4-Difluoro-10-phenylphenanthrene (56g)

9-(3,5-Difluorophenyl)phenanthrene (57g)



56g **57g**

The general procedure for the intramolecular arylation reaction and for the aromatization was followed: bromoarene **55g** (105 mg, 0.281 mmol), $Pd(OAc)_2$ (3.5 mg, 0.016 mmol), **58** (11.1 mg, 0.029 mmol), K_2CO_3 (77.8 mg, 0.562 mmol), DMA (1.5 mL), 135 ºC, 16 h, DDQ (637 mg, 2.81 mmol), toluene (5 mL) reflux 24 h. The final residue was purified by column chromatography (SiO_2, hexane) to give a 19:1 mixture of regioisomers **56g**/**57g** (62 mg, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (d, *J* = 8.6 Hz, 1H **56g**), 8.78 (d, *J* = 8.2 Hz, 1H **57g**), 8.72 (d, *J* = 8.2 Hz, 1H **57g**), 7.91-7.86 (m, 1H **56g** + 1H **57g**), 7.74 (s, 1H **56g**), 7.73-7.46 (m, 7H **56g** + 6H **57g**), 7.38 (ddd, *J* = 10.2, 2.6, 1.2 Hz, 1H **56g**), 7.18 (ddd, *J* = 13.7, 8.2, 2.6 Hz, 1H **56g**), 7.09 (m, 2H **57g**), 6.92 (tt, *J* = 9.0, 2.3 Hz, 1H **57g**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.87 (dd, *J* = 249.3, 12.7 Hz) **57g**, 162.04 (dd, *J* = 255.9, 12.4 Hz) **56g**, 159.96 (dd, *J* = 246.4, 14.9 Hz) **56g**, 140.04 **56g**, 137.66 (t, *J* = 3.7 Hz) **56g**, 134.60 (dd, *J* = 9.6, 5.9 Hz) **56g**, 131.52 **56g**, 131.13 **57g**, 130.64 **57g**, 130.26 **57g**, 130.03 **56g**, 129.86 **56g** + **57g**, 128.79 **57g**, 128.73 **56g**, 128.56 **56g** + **57g**, 127.80 **56g** + **57g**, 127.74 **56g**, 127.67 **57g**, 127.54 **56g**, 127.51 **56g** 127.13 **57g**, 127.06 **56g** + **57g**, 126.98, **56g** 126.96 **56g**, 126.81 **57g**, 126.79 **56g**, 123.08 **57g**, 122.59 **57g**,116.77 (dd, *J* = 8.8, 2.9 Hz) **56g**, 113.10 (dd, *J* = 18.3, 7.3 Hz) **57g**, 107.90 (dd, *J* = 22.0, 3.7 Hz) **56g**, 103.24 (dd, *J* = 27.4, 27.1 Hz) **56g**, 102.86 (t, *J* = 25.2 Hz) **57g**. HRMS-CI *m/z* calcd for $C_{20}H_{13}F_2$ $[M+H]^+$ 291.0985, found 291.0992.

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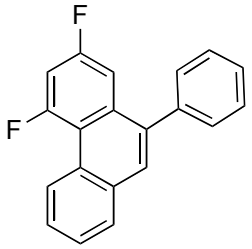
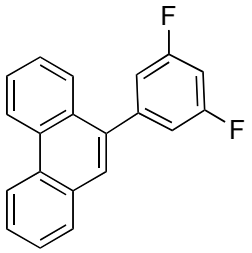
2,4-Difluoro-10-phenylphenanthrene (56g)



A careful purification by column chromatography (SiO_2, hexane) gave pure **56g** as a white solid: mp 106-107 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (d, *J* = 8.5 Hz, 1H), 7.90 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.74 (s, 1H), 7.70 (tt, *J* = 7.0, 1.5 Hz, 1H), 7.66-7.62 (m, 1H), 7.55-7.46 (m, 5H), 7.38 (ddd, *J* = 10.2, 2.6, 1.2 Hz, 1H) 7.18 (ddd, *J* = 13.7, 8.2, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.05 (dd, *J* = 255.9, 12.4 Hz), 159.96 (dd, *J* = 246.4, 14.9 Hz), 140.04, 137.67 (t, *J* = 3.7 Hz), 134.60 (dd, *J* = 9.6, 5.9 Hz), 131.52, 130.03, 129.86, 128.73, 128.56, 127.80, 127.74, 127.55, 127.52, 127.05, 126.98, 126.96, 126.79, 116.77 (dd, *J* = 8.8, 3.0 Hz), 107.90 (dd, *J* = 22.0, 3.7 Hz), 103.24 (dd, *J* = 27.4, 27.1 Hz).

9-(3,5-Difluorophenyl)phenanthrene (57g)



A careful purification by column chromatography (SiO_2, hexane) gave an enriched fraction containing a 10:1 mixture **57g/56g**. ^{1}H NMR (400 MHz, $CDCl_3$, for the major regioisomer) δ 8.79 (d, *J* = 8.2 Hz, 1H), 8.73 (d, *J* = 8.2 Hz, 1H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.74-7.62 (m, 4H), 7.60-7.56 (m, 1H), 7.53-7.48 (m, 1H), 7.09 (m, 2H), 6.92 (tt, *J* = 9.0, 2.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, for the major regioisomer) δ 162.87 (dd, *J* = 249.3, 12.7 Hz), 144.08 (t, *J* = 9.4 Hz), 131.15, 130.65, 130.29, 129.86, 128.80, 128.56, 127.80, 127.67, 127.13, 127.07, 126.83, 126.80, 126.29, 123.08, 122.59, 113.10 (dd, *J* = 18.3, 7.1 Hz),

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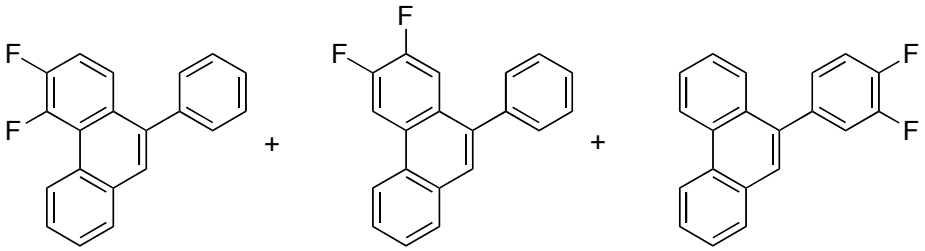
3,4-Difluoro-10-phenylphenanthrene (56h)

2,3-Difluoro-10-phenylphenanthrene (56'h)

9-(3,4-Difluorophenyl)phenanthrene (57h)



56h **56'h** **57h**

The general procedure for the intramolecular arylation reaction and for the aromatization was followed: bromoarene **55h** (115 mg, 0.365 mmol), $Pd(OAc)_2$ (5.3 mg, 0.024 mmol), **58** (14.1 mg, 0.077 mmol), K_2CO_3 (120 mg, 0.867 mmol), DMA (1.5 mL), 135 ºC, 16 h, DDQ (251 mg, 1.10 mmol), toluene (5 mL) reflux 48 h. The final residue was purified by column chromatography (SiO_2, hexane) to give a 6.8:1.4:1 mixture of three **56h**/**56'h**/**57h** regioisomers (57 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (d, *J* = 7.6 Hz, 1H **56h**), 8.79 (d, *J* = 8.2 Hz, 1H **57h**), 8.73 (d, *J* = 8.2 Hz, 1H **57h**), 8.51-8.44 (m, 2H **56'h**), 7.92-7.89 (m, 1H **56h** + 1H **56'h** + 1H **57h**), 7.85 (d, *J* = 7.4 Hz, 1H **57h**), 7.74-7.58 (m, 4H **56h** + 4H **56'h** + 4H **57h**), 7.55-7.46 (m, 5H **56h** + 5H **56'h** + 1H **57h**), 7.40-7.26 (m, 1H **56h** + 3H **57h**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.01 (dd, *J* = 253.8, 13.5 Hz) **56h**, 148.97 (dd, *J* = 247.6, 14.6 Hz) **56'h**, 140.18 **56h**, 140.02 **56'h**, 137.93 (t, *J* = 2.2 Hz) **56h**, 137.75 **57h**, 136.56 **57h**, 132.32 **56h**, 131.46 **56'h**, 131.23 **57h**, 130.64 **57h**, 130.26 **57h**, 130.09 **57h**, 129.97 **56h**, 129.80 **56'h**, 129.34 (t, *J* = 2.4 Hz) **56h**, 129.04 **56'h**, 129.00 **57h**, 128.85 **56'h**, 128.72 **57h**, 128.70 **57h**, 128.61 **56h**, 128.57 **56'h**, 128.43 **56h**, 128.36 **57h**, 128.13 **56h**, 127.83 **56'h**, 127.81 **57h**, 127.78 **56'h**, 127.72 **56'h**, 127.67 **56h**, 127.65 **56h**, 127.63 **56h**, 127.53 **56'h**, 127.27 **56h**, 127.23 **56'h**, 127.17 **56h**, 127.15 **56h**, 127.01 **56'h**, 126.98 **56'h**, 126.96 **57h**, 126.73 **57h**, 126.69 **57h**, 126.35 **57h**, 126.16 **57h**, 126.12 **57h**, 126.10 **57h**, 125.96 **57h**, 123.04 **57h**, 122.88 (dd, *J* = 7.5, 4.8 Hz) **56h**, 122.54 **56'h**, 121.45 (d, *J* = 5.8 Hz) **56h**, 119.03 (d, *J* = 16.8 Hz) **57h**, 117.15 (d, *J* = 16.9 Hz) **57h**, 115.46 (d, *J* = 19.0 Hz) **56h**, 113.92 (dd, *J* = 16.7, 2.8 Hz) **56'h**, 110.48 (dd, *J* = 14.8, 4.4 Hz) **56'h**. HRMS-CI *m/z* calcd

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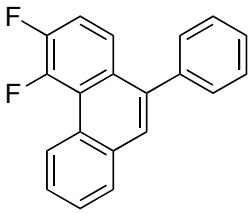
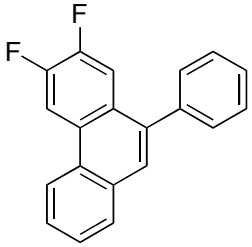
3,4-Difluoro-10-phenylphenanthrene (56h)



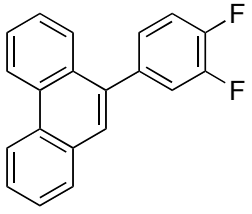
A careful purification by column chromatography (SiO_2, hexane) gave pure **56h** as a white solid: mp 114-115 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 7.3 Hz, 1H), 7.73-7.65 (m, 4H), 7.55-7.46 (m, 5H), 7.36 (q, J = 8.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.01 (dd, J = 253.8, 13.5 Hz), 148.97 (dd, J = 247.6, 14.6 Hz), 140.17, 137.92 (t, J = 2.2 Hz), 132.30, 129.97, 129.34 (t, J = 2.4 Hz), 128.60, 128.42, 128.12, 127.66, 127.63, 127.61, 127.51, 127.16, 127.13, 122.86 (dd, J = 7.4, 4.4 Hz), 121.43 (d, J = 5.8 Hz) 115.44 (d, J = 19.0).

2,3-Difluoro-10-phenylphenanthrene (56'h)



A careful purification by column chromatography (SiO_2, hexane) gave an enriched fraction of **56'h**: ^{1}H NMR (400 MHz, $CDCl_3$, for the major regioisomer) δ 8.52-8.45(m, 2H), 7.92-7.89 (m, 1H), 7.71-7.62 (m, 4H), 7.55-7.46 (m, 5H).

9-(3,4-Difluorophenyl)phenanthrene (57h)



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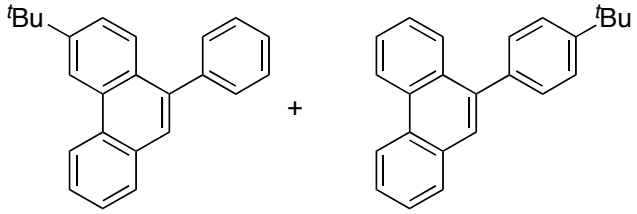
A careful purification by column chromatography (SiO_2, hexane) gave an enriched fraction of **57h**: ^{1}H NMR (400 MHz, $CDCl_3$, for the major regioisomer) δ 8.78 (d, J = 8.2 Hz, 1H), 8.72 (d, J = 8.2 Hz, 1H), 7.90 (d, J = 7.7 Hz, 1H), 7.85 (d, J = 8.5 Hz, 1H), 7.71-7.62 (m, 4H), 7.60-7.49 (m, 1H), 7.59-7.26 (m, 3H).

3-*tert*-Butyl-10-phenylphenanthrene (56i)

9-(4-*tert*-Butylphenyl)phenanthrene (57i)



56i **57i**

The general procedure for the intramolecular arylation reaction and for the aromatization was followed: bromoarene **55i** (101 mg, 0.256 mmol), $Pd(OAc)_2$ (2.8 mg, 0.013 mmol), **58** (9.7 mg, 0.025 mmol), K_2CO_3 (70.2 mg, 0.508 mmol), DMA (2.0 mL), 135 ºC, 16 h, DDQ (173 mg, 0.762 mmol), toluene (5 mL) reflux 3 h. The final residue was purified by column chromatography (SiO_2, hexane) to give a 1:1.5 mixture of regioisomers **56i/57i** (53 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82-8.79 (m, 1H **57i** + 1H **56i**), 8.75 (d, J = 8.2 Hz, 1H **57i**), 7.91-7.88 (m, 1H **57i** + 2H **56i**), 7.72-7.47 (m, 9H **57i** + 9H **56i**) 1.50 (s, 9H **56i**), 1.43 (s, 9H **57i**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.23 **57i**, 149.11 **56i**, 140.97 **56i**, 138.73 **57i**, 138.51 **56i**, 137.77 **57i**, 131.80 **56i**, 131.65 **57i**, 131.25 **57i**, 130.63 **57i**, 130.29 **56i**, 130.11 **56i**, 130.03 **56i**, 129.88 **57i**, 129.71 **56i**, 129.03 **56i**, 128.70 **57i**, 128.60 **57i**, 128.25 **56i**, 127.49 **57i**, 127.28 **56i**, 127.06 **57i**, 126.78 **57i**, 126.63 **56i**, 126.43 **57i**, 126.40 **57i**, 126.36 **56i**, 126.31 **56i**, 125.19 **57i**, 124.77 **56i**, 122.85 **57i**, 122.49 **57i**, 122.38 **56i**, 118.53 **56i**, 35.13 **56i**, 34.64 **57i**, 31.48 **57i**, 31.46 **56i**.

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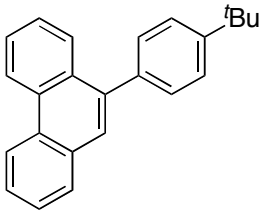
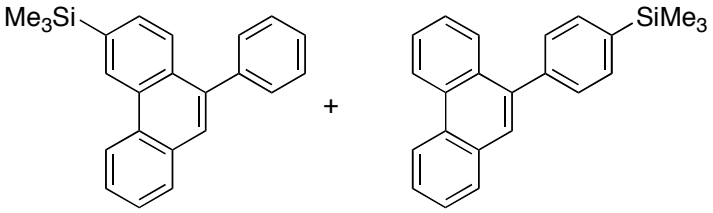
9-(4-*tert*-Butylphenyl)phenanthrene (57i)



The general procedure for the Suzuki coupling was followed**:** 9-bromophenantrene (199 mg, 0.743 mmol), KF (268 mg, 4.62 mmol), $Pd(dba)_2$ (78.4 mg, 0.205 mmol), 2-(dicyclohexylphosphino)biphenyl (131 mg, 0.345 mmol) and 4-*tert*-butylphenylboronic acid (397 mg, 2.23 mmol), toluene (5 mL) sat. solution NaCl (15 mL), Et_2O (3 x 30 mL). The residue was chromatographed (SiO_2, hexane) to give **57i** (152 mg, 63%) as a white solid: mp 147-149 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 8.2 Hz, 1H), 8.73 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.70-7.49 (m, 9H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.26, 138.72, 137.76, 131.64, 131.24, 130.62, 129.88, 129.70, 128.60, 127.48, 127.05, 126.77, 126.44, 126.41, 126.36, 125.20, 122.85, 122.50, 34.64, 31.46. HRMS-CI *m/z* calcd for $C_{24}H_{23}$ $[M+H]^+$ 311.1800, found 311.1799.

3-(Trimethylsilyl)-10-phenylphenanthrene (56j)

9-(4-(Trimethylsilyl)phenyl)phenanthrene (57j)



56j **57j**

The general procedure for the intramolecular arylation reaction and for the aromatization was followed: bromoarene **55j** (58.1 mg, 0.141 mmol), $Pd(OAc)_2$ (2.4 mg, 0.011 mmol), **58** (6.7 mg, 0.017 mmol), K_2CO_3 (52.7 mg, 0. 301 mmol), DMA (1.5 mL), 135 ºC, 16 h, DDQ (103 mg, 0.455 mmol), toluene (5 mL) reflux 4 h. The final residue was purified by column chromatography (SiO_2, hexane) to give a 1:1.3 mixture of regioisomers **56j/57j** (34 mg, 74%) as a colorless oil:

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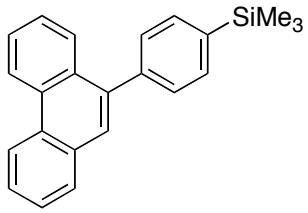
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H **56j**) 8.83-8.79 (m, 1H **56j** + 1H **57j**), 8.74 (d, *J* = 8.1 Hz, 1H **57j**), 7.98 (d, *J* = 8.2 Hz, 1H **57j**) 7.93-7.89 (m, 2H **56j** +1H **57j),** 7.72-7.47 (m, 9H **56j** + 9H **57j**) 1.50 (s, 9H **56j**), 1.43 (s, 9H **57j**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.17 **57j**, 140.75 **56j**, 139.37 57j, 138.74 **57j**, 138.69 **56j**, 138.42 **56j**, 133.30 **57j**, 131.63 **56j**, 131.57 **57j**, 131.39 **56j**, 131.06 **57j**, 130.91 **56j**, 130.62 **57j**, 130.03 **56j**, 129.93 **57j**, 129.38 **57j**, 128.70 **56j**, 128.66 **57j**, 128.27 **56j**, 128.11 **56j**, 127.83 **56j**, 127.51 **57j**, 127.33 **56j**, 126.97 **57j**, 126.82 **57j**, 126.74 **56j**, 126.56 **57j**, 126.46 **57j**, 126.43 **57j**, 125.94 **56j**, 122.88 **57j**, 122.52 **57j**, 122.38 **56j**, -0.96 **56j**, -1.01 **57j**. HRMS-CI *m/z* calcd for $C_{23}H_{22}SiBr$ $[M+]^+$ 326.1491, found. 326.1492.

9-(4-(Trimetylsilyl)phenyl)phenanthrene (57j)



The general procedure for Suzuki coupling was followed: 9-bromophenantrene (118 mg, 0.459 mmol), KF (68.3 mg, 1.28 mmol), $Pd(dba)_2$ (2.1 mg, 0.052 mmol), 2-(dicyclohexylphosphino)biphenyl (13.7 mg, 0.039 mmol), toluene (5 mL), 4-(trimethylsilyl)phenylboronic acid (103 mg, 0.530 mmol), NaCl sat. solution (3 x 15 mL) and Et_2O (3 x 20 mL). The residue was chromatographed (SiO_2, hexane) to give **57j** (91 mg, 62%) as a white solid: mp 105-107 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (d, *J* = 8.3 Hz, 1H), 8.75 (d, *J* = 8.2 Hz, 1H), 8.00 (d, *J* = 7.9 Hz, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.73-7.55 (m, 9H), 0.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.18, 139.36, 138.75, 133.30, 131.57, 131.06, 130.62, 129.94, 129.39, 128.66, 127.51, 126.97, 126.82, 126.56, 126.47, 126.44, 122.88, 122.52, -1.01. HRMS-CI *m/z* calcd for $C_{23}H_{23}Si$ $[M+H]^+$ 327.1569, found 327.1567.

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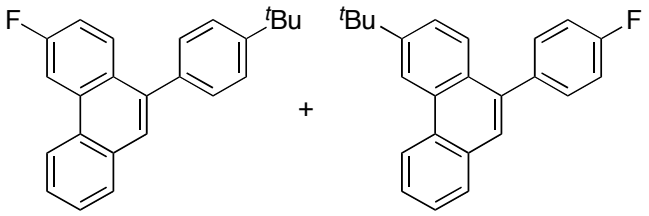
3'-Fluoro-10-(4-*tert*-butylphenyl)phenanthrene (56k)

3-*tert*-Butyl-10-(4'-fluorophenyl)phenanthrene (57k)



56k **57k**

The general procedure for the intramolecular arylation reaction and for the aromatization was followed: bromoarene **55k** (70.9 mg, 0.142 mmol), $Pd(OAc)_2$ (1.9 mg, 0.009 mmol), **58** (6.8 mg, 0.018 mmol), K_2CO_3 (48.3 mg, 0.349 mmol), DMA (1.5 mL), 135 ºC, 16 h, DDQ (118 mg, 0.520 mmol), toluene (5 mL) reflux 20 h. The final residue was purified by column chromatography (SiO_2, hexane) to give a 2.3:1 mixture of regioisomers **56k**/**57k** (46 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77-74 (m, 2H **57k**), 8.57-8.55 (m, 1H **56k**), 8.36 (dd, *J* = 11.1, 2.7 Hz, 1H **56k**), 7.96 (dd, *J* = 9.2, 6.1 Hz, 1H **56k**), 7.88-7.86 (m, 1H **56k** + 1H **57k**), 7.79 (d, *J* = 8.8 Hz, 1H **57k**) 7.67-7.44 (m, 7H **56k** + 6H **57k**), 7.27 (ddd, *J* = 8.0, 3.0, 1.2 Hz, 1H **56k**), 7.19 (tt, *J* = 8.6, 2.0 Hz, 2H **57k**), 1.43 (s, 9H **57k**), 1.33 (s, 9H **56k**); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.28 (*J* = 246.0 Hz) **57k**, 161.46 (*J* = 245.8 Hz) **56k**, 150.46 **56k**, 149.31 **57k**, 138.40, 137.51, 137.41, 136.81 (*J* = 3.2 Hz) **57k**, 132.38 (*J* = 8.1 Hz) **56k**, 132.34, 131.53 (*J* = 8.0 Hz) **57k**, 131.49, 130.29, 129.63, 129.38 (*J* = 8.8 Hz) **56k**, 129.34, 129.30, 129.25, 128.98, 128.67, 128.65, 128.44, 128.32, 127.97 (*J* = 1.5 Hz) **56k**, 127.39, 126.92, 127.39, 126.92, 126.69, 126.66, 126.64, 126.48, 126.45, 126.37, 125.29, 124.88, 122.71**56k**, 122.41 **57k**, 118.61 **57k**, 115.23 (d, *J* = 22.7 Hz), 115.17 (d, *J* = 21.2 Hz), 107.88 (d, *J* = 21.9 Hz) **56k**, 35.15 **57k**, 34.67 **56k**, 31.48 **57k**, 31.44 **56k**. HRMS-CI *m/z* calcd for $C_{24}H_{21}F$ $[M]^+$ 328.1627, found 328.1622.

General procedure for the intramolecular arylation reaction of substrate 55f using different bases, additives and ligands: A solution of the bromoarene **55**, $Pd(OAc)_2$ (5 mol%), ligand (10 mol% when monodentate ligands or 5 mol% when bidentate ligands were used), base (2.5 equiv) and additive (0.3 equiv) in anhydrous

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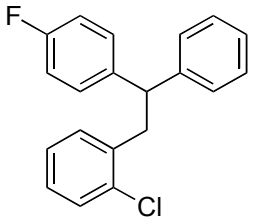
DMA was heated between 80 and 135 ºC (see *Tables 4, 5, 6, and 9*). Once the arylation was completed the reaction mixture was cooled to room temperature. A saturated solution of NaCl was added and the organic layer was extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4, filtered and the solvent was evaporated. After being analyzed by ^1H NMR to determine the amount of reduction product **68**, the crude mixture was aromatized with DDQ.

3.1.4 New Optimized Conditions for the Pd-Catlyzed Arylation

General procedure for the intramolecular arylation reaction of substrate 55f or 55l using different phosphazenes as the base: A solution of the bromoarene **55**, $Pd(OAc)_2$ (5 mol%) and **58** (10 mol%) or dppf (5 mol%) were dissolved in anhydrous DMA. Phosphazene base (2.5 equiv) was added dropwise *via* syringe and the reaction mixture was heated at 40 to 135 ºC (see *Tables 7 and 8*). Once the arylation was completed the reaction mixture was cooled to room temperature and the solvent was evaporated. The residue was filtered through using hexane as eluent. After being analyzed by ^1H NMR to determine the amount of reduction product **68**, the crude mixture was aromatized with DDQ.

General procedure for the aromatization: A solution of the crude arylation product and DDQ (3 equiv) in toluene was heated to reflux for 16 h. The reaction mixture was cooled to room temperature, toluene was evaporated and the reaction crude was filtered through silica using hexane as eluent. The solvent was evaporated and the residue was chromatographed (SiO_2, hexane) to give the mixture **56** and **57**.

1-Chloro-2-(2-(4-fluorophenyl)-2-phenylethyl)benzene (80)



The general procedure for the synthesis of **55** was followed: 1,2-dibromoethane (0.09 mL, 1.01 mmol), 2-bromobenzylbromide (1.58 mL, 12.1 mmol), Mg (2.07 g,

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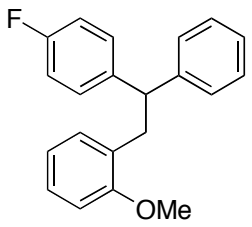
water (for the first extraction 150 mL), Et_2O (for the first extraction 3 x 150 mL), triethylsilane (9.54 mL, 7.12 mmol), $BF_3{\cdot}Et_2O$ (4.51 mL, 35.6 mmol), CH_2Cl_2 (solvent, 65 mL), sat. solution NH_4Cl (for the second extraction, 100 mL), CH_2Cl_2 (for the second extraction, 3 x 100 mL). The residue was chromatographed (SiO_2, hexane) to give **80** (1.33 g, 60%, for the two steps) as a white solid: mp 49-50 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.33 (m, 3H), 7.18-7.20 (m, 3H), 7.11-7.16 (m, 2H), 7.07 (dt, *J* = 7.6, 1.5 Hz, 1H), 6.90-6.98 (m, 3H), 6.76 (dd, *J* = 7.6, 1.2 Hz, 1H), 4.36 (t, *J* = 7.8 Hz, 1H), 3.38-3.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.59, 160.17, 143.86, 139.68 (d, *J* = 3.3 Hz), 137.38, 134.16, 131.35, 129.56, 129.48, 129.38, 128.41, 127.97, 127.53, 126.41, 126.29, 115.16, 114.95, 49.84, 39.87; ^{19}F NMR ($CDCl_3$, 376.5 MHz) δ -117.0.

1-(2-(4-Fluorophenyl)-2-phenylethyl)-2-methoxybenzene (83)



The general procedure for the synthesis of **55** was followed: 1,2-dibromoethane (0.08 mL, 0.98 mmol), 2-methoxybenzylbromide (2.36 g, 11.7 mmol), Mg (1.99 g, 82.0 mmol), Et_2O (solvent, 2 x 40 mL), 4-fluorobenzophenone (1.42 g, 6.87 mmol), water (for the first extraction 150 mL), Et_2O (for the first extraction 3 x 150 mL), triethylsilane (5.90 mL, 36.6 mmol), $BF_3{\cdot}Et_2O$ (2.79 mL, 22.0 mmol), CH_2Cl_2 (solvent, 40 mL), sat. solution NH_4Cl (for the second extraction, 100 mL), CH_2Cl_2 (for the second extraction, 3 x 100 mL). The residue was chromatographed (SiO_2, 10:1 hexane/CH_2Cl_2) to give **83** (1.23 g, 62% for the two steps) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09-7.26 (m, 8H), 6.89 (t, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 8.8 Hz, 2H), 6.70 (t, *J* = 7.4 Hz, 1H), 4.31 (t, *J* = 7.7 Hz, 1H), 3.75 (s, 3H), 3.26-3.36 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.43, 160.01, 157.49, 144.76, 140.51 (d, *J* = 3.0 Hz), 130.66, 129.60, 129.52, 128.24, 128.03, 127.22, 126.10, 120.07, 114.92, 114.71, 110.10, 55.18, 50.19, 36.52.

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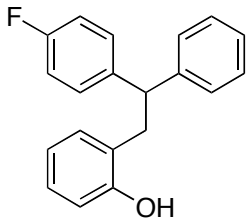
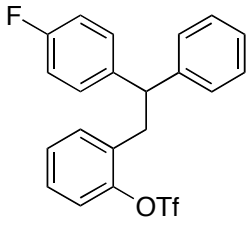
2-(2-(4-Fluorophenyl)-2-phenylethyl)phenol (84)



A solution of BBr_3 (1.0 M in CH_2Cl_2, 18.57 mL, 18.57 mmol) was added over a solution of 1-(2-(4-fluorophenyl)-2-phenylethyl)-2-methoxybenzene (**83**) (1.14 g, 3.71 mmol) in CH_2Cl_2 (40 mL) at r.t. and the mixture was stirred for 65 h at r.t. After cooling to 0 ºC, water was added very slowly and the organic layer was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts were washed with water dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, 1:1 hexane/ CH_2Cl_2) to give **84** (935 mg, 86%) as a white solid: mp 102-103 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) 7.24-7.28 (m, 2H), 7.13-7.21 (m, 5H), 7.02 (dt, J = 7.7, 1.7 Hz, 1H), 6.92 (t, J = 8.7 Hz, 2H), 6.82 (dd, J = 7.4, 1.2 Hz, 1H), 6.72 (dt, J = 7.4, 1.0 Hz, 1H), 6.67 (dd, J = 7.9, 1.0 Hz, 1H), 4.45 (s, 1H), 4.32 (t, J = 7.7 Hz, 1H), 3.27-3.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.55, 160.12, 153.50, 144.42, 140.23 (d, J = 3.4 Hz), 131.13, 129.49, 129.41, 128.45, 127.92, 127.39, 126.37, 126.24, 120.72, 115.37, 115.24, 114.95, 50.38, 36.62. HRMS-CI *m/z* calcd for $C_{20}H_{16}FO$ $[M-H]^+$ 291.1185, found 291.1177.

2-(2-(4-Fluorophenyl)-2-phenylethyl)phenyl Trifluoromethanesulfonate (85)



2,6-Lutidine (0.69 mL, 5.92 mmol) and Tf_2O (1.00 mL, 5.92 mmol) were added over a solution of the phenol **84** (0.87 g, 2.96 mmol) and DMAP (0.02 g, 0.14 mmol) in anhydrous CH_2Cl_2 (60 mL) at -30 ºC and the reaction mixture was slowly warmed up to 0 ºC and stirred at 0 ºC for 24 h. Water (50 mL) was added and

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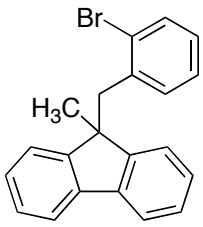
extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, 5:1 hexane/CH_2Cl_2) to give **85** (1.13 g, 90%) as a colorless oil.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.28 (m, 3H), 7.12-7.22 (m, 7H), 7.00 (dd, J = 7.9, 1.2 Hz, 1H), 6.93 (t, J = 8.7 Hz, 2H), 4.29 (t, J = 8.0 Hz, 1H), 3.37-3.47 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.70, 160.27, 148.10, 143.18, 139.12 (d, J = 3.0 Hz), 132.69, 132.04, 129.40, 129.32, 128.54, 128.16, 128.00, 127.80, 126.63, 121.19, 115.33, 115.13, 50.53, 36.40; ^{19}F NMR (376.5 MHz, $CDCl_3$,) δ -75.0, -117.7 HRMS-CI *m/z* calcd $C_{20}H_{17}FO$ $[M-SO_2CF_3]^+$ 291.1185, found 291.1197.

3.1.6 Investigation on the Enantioselective Arylation Reaction

The synthesis of 9,9-bis(2-bromobenzyl)-9*H*-fluorene (**90**) and 15,16-dihydrophenanthro[1,10-*ef*]acephenanthrylene (**91**) have been already reported.[110]

9-(2-Bromobenzyl)-9-methyl-9*H*-fluorene (88)



Bromobenzyl fluorene (900 mg, 2.68 mmol) in DMF (5 mL) was added over a suspension of NaH (60% in mineral oil, 107 mg, 2.68 mmol) in DMF (10 mL) at r.t. After 5 min, MeI was added dropwise and the reaction mixture was stirred at r.t. for 30 min. Water (20 mL) was added slowly and organic layer was extracted with AcOEt (3 x 50 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, 6:1 hexane/CH_2Cl_2) to give **88** (189 mg, 20%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.4 Hz, 2H), 7.36 (dd, J = 7.7, 1.4 Hz, 1H), 7.19-7.29 (m, 6H), 6.86-6.94 (m, 2H), 6.70 (dd, J = 7.4, 1.9 Hz, 1H), 3.30 (s, 2H), 1.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.17, 139.73, 137.64, 132.68, 131.43, 127.84, 127.14, 126.88, 126.35, 126.21, 123.82, 119.81, 51.29, 44.61, 25.23. HMRS-ESI *m/z* calcd for $C_{21}H_{18}{}^{79}Br$ $[M+H]^+$ 349.0592, found 349.0595.

8a-Methyl-8,8a-dihydrobenzo[*e*]acephenanthrylene (89)

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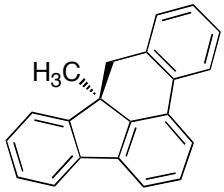

General procedure for the arylation of substrates 88 and 90 using different ligands: A mixture of 9-(2-bromobenzyl)-9-methyl-9*H*-fluorene **(88)** (49.9 mg, 0.14 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), (*R*)-Josiphos (9.2 mg, 0.014 mmol) and K_2CO_3 (52.3 mg, 0.36 mmol) in anhydrous DMA was heated at 135 ºC for 6 h. Saturated NaCl solution (20 mL) was added and the organic layer was extracted with AcOEt (3 x 25 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, hexane) to give **89** (41 mg, 90%) as a white solid: mp 105-106 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.1 Hz, 1H), 7.77 (d, *J* = 7.1 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 7.3 Hz, 1H), 7.27-7.44 (m, 6H), 3.22 (d, *J* = 14.7 Hz, 1H), 2.88 (d, *J* = 14.7 Hz, 1H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.35, 149.43, 140.51, 138.30, 136.89, 133.83, 131.68, 130.06, 128.33, 128.05, 127.23, 127.06, 123.46, 123.09, 121.16, 120.94, 119.10, 45.59, 38.69, 23.85. HRMS-ESI *m/z*: calcd for $C_{21}H_{17}$ $[M+H]^+$ 269.1330, found 269.1319.

3.2. Synthesis of non-planar PAHs

3.2.1 Bromobenzyl Fluorene (87)

The synthesis of 9-(2-bromophenylmethyl)fluorene (**87**) and benzo[*e*]acephenanthry-lene (**95**) have been already reported.[110]

General procedure for the intramolecular arylation reaction of substrate 87 using different ligands and additives: A solution of the bromoarene **87**, $Pd(OAc)_2$ (5 mol%), ligand (10 mol% when monophosphine **58** is used or 5 mol% when diphosphines are used), K_2CO_3 (2.5 equiv) and pivalic acid (0.3 equiv) in anhydrous DMA was heated between 40 and 100 ºC (see *Table 14*). Once the arylation was completed the reaction mixture was cooled to room temperature. A saturated solution of NaCl was added and organic layer was extracted with EtOAc. The

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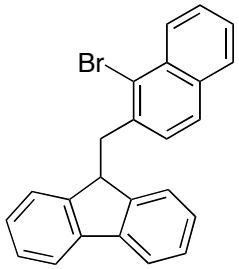
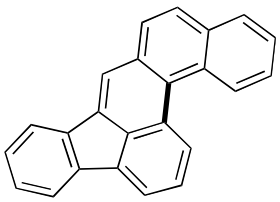
combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, hexane) to give **95**.

9-((1-Bromonaphthalen-2-yl)methyl)-9*H*-fluorene (94)



n-BuLi (2.5 M in hexanes, 0.75 mL, 1.87 mmol) was added over a solution of fluorene (**86**) (288 mg, 1.70 mmol) in anhydrous THF (8.5 mL) at -80 ºC. The reaction mixture was stirred at -80 ºC for 3 h. Bromonaphthyl bromide (**97**) (407 mg, 1.36 mmol) in anhydrous THF (6.8 mL) was added and the reaction mixture was allowed to get r.t. overnight. Saturated NaCl solution (20 mL) was added and the organic layer was extracted with CH_2Cl_2 (3 x 25 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, 4:1 hexane/CH_2Cl_2) to give **94** (465 mg, 71%) as a white solid: mp 148-149 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.78 (d, J = 7.8 Hz, 3H), 7.62-7.66 (m, 1H), 7.53-7.57 (m, 1H), 7.35-7.39 (m, 1H), 7.28 (d, J = 8.3 Hz, 1H), 7.16-7.23 (m, 5H), 4.54 (t, J = 7.8 Hz, 1H), 3.40 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.81, 140.77, 137.62, 133.57, 132.69, 129.85, 128.14, 127.45, 127.32, 127.17, 126.71, 126.21, 125.06, 124.81, 119.85, 46.80, 42.13. HRMS-ESI *m/z* calcd for $C_{24}H_{18}{}^{79}Br$ $[M+H]^+$ 385.0592, found 385.0577.

Dibenzo[*e*,*l*]acephenanthrylene (96)



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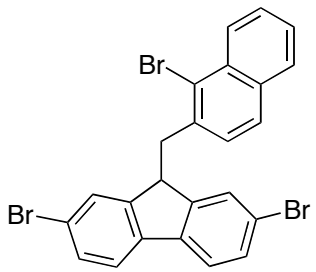
General procedure for the intramolecular arylation reaction of substrate 94 using different bases, additives and ligands: A mixture of **94** (48.2 mg, 0.12 mmol), $Pd(OAc)_2$ (1.4 mg, 0.006 mmol), dppf (3.5 mg, 0.006 mmol), *t*-$BuCO_2H$ (3.7 mg, 0.036 mmol) and K_2CO_3 (44.6 mg, 0.31 mmol) in anhydrous DMA was heated at 80 ºC for 19 h. Saturated NaCl solution (20 mL) was added and the organic layer was extracted with AcOEt (3 x 25 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. Crude product in toluene (2 mL) was added over DDQ (86.9 mg, 0.37 mmol) in toluene (3 mL) and the mixture was heated at 110 ºC overnight. Toluene was evaporated under reduced pressure and crude product was purified by chromatography (SiO_2, hexane) to give **96** (30 mg, 79%) as a pale yellow solid: mp 152-153 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (d, *J* = 8.5 Hz, 1H), 8.99 (d, *J* = 8.5 Hz, 1H), 8.27 (s, 1H), 7.89-8.02 (m, 6H), 7.80 (dd, *J* = 8.5, 7.0 Hz, 1H), 7.71-7.75 (m, 1H), 7.61-7.65 (m, 1H), 7.38-7.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.56, 138.26, 137.34, 135.89, 133.75, 133.33, 132.95, 131.22, 128.71, 128.46, 128.33, 128.03, 127.88, 127.58, 127.54, 127.08, 126.57, 125.99, 122.00, 121.72, 121.26, 119.37. HRMS-ESI *m/z* calcd for $C_{24}H_{15}$ $[M+H]^+$ 303.1174, found 303.1159

2,7-Dibromo-9-((1-bromonaphthalen-2-yl)methyl)-9*H*-fluorene (100)



100

n-BuLi (2.5 M in hexanes, 0.69 mL, 1.73 mmol) was added over a solution of 2,7-dibromofluorene (**99**) (521 mg, 1.58 mmol) in anhydrous THF (8.5 mL) at -80 ºC. The reaction mixture was stirred at -80 ºC for 5 min and 1-bromo-2-(bromomethyl)naphthalene (520 mg, 1.73 mmol) in anhydrous THF (6.5 mL) was added and the reaction mixture was stirred at -80 ºC overnight. Saturated NaCl

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(3 x 25 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was evaporated. The residue was chromatographed (SiO_2, 5:1 hexane/CH_2Cl_2) to give **94** (594 mg, 69%) as a pale yellow solid: mp 183-184 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.5 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.64-7.68 (m, 1H), 7.55-7.60 (m, 1H), 7.48-7.51 (m, 1H), 7.29 (s, 2H), 7.21 (d, *J* = 8.3 Hz, 1H), 4.50 (t, *J* = 7.7 Hz, 1H), 3.34 (d, *J* = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.46, 138.77, 136.44, 133.74, 132.69, 130.56, 129.57, 128.47, 128.27, 127.67, 127.35, 127.25, 126.46, 124.94, 121.23, 120.96, 46.72, 41.90. HRMS-ESI *m/z* calcd for $C_{24}H_{15}{}^{79}Br_3$ $[M]^+$ 539.8718, found 539.8688.

3.2.4 Trisubstituted Truxene Derivatives

The synthesis of (5*S*,10*S*,15*S*)-5,10,15-tris(2-bromobenzyl)-10,15-dihydro-5*H*-diindeno[1,2-*a*:1',2'-*c*]fluorene (**22**) 2,7,12-tribromo-5,10,15-tris((1-bromonaphthalen-2-yl)methyl)-10,15-dihydro-5H-diindeno[1,2-a:1',2'-c]fluorene (**24**), benzo[1,2-*e*:3,4-*e′*:5,6-*e″*]triacephenanthrylene (**23**), Benzo[1,2-e:3,4-e':5,6-e'']tribenzo[l]acephenanthrylene (**25**) and 2,7,12-tribromo-10,15-dihydro-5*H*-diindeno[1,2-*a*:1',2'-*c*]fluorene (**103**) have been already reported.[142]

[142] (a) de Frutos, Ó.; Gómez-Lor, B.; Granier, T.; Monge, M. Á.; Gutiérrez-Puebla, E.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **1999**, *38*, 204-207. (b) Gómez-Lor, B.; de Frutos, Ó.; Ceballos, P. A.; Granier, T.; Echavarren, A. M. *Eur. J. Org. Chem.* **2001**, 2107-2114. (c) Gómez-Lor, B.; González-Cantalapiedra, E.; Ruiz, M.; de Frutos, Ó.; Cárdenas, D. J.;

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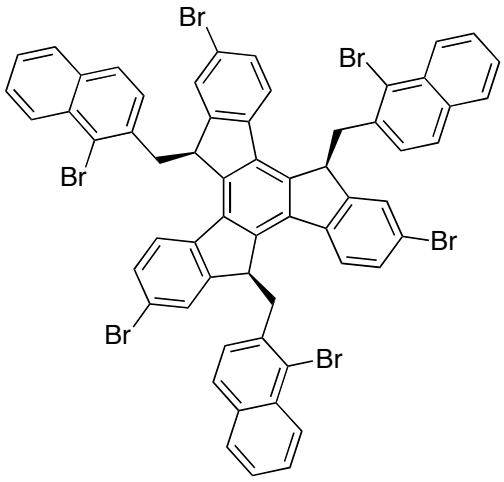
2,7,12-Tribromo-5,10,15-tris((1-bromonaphthalen-2-yl)methyl)-10,15-dihydro-5*H*-diindeno[1,2-*a*:1',2'-*c*]fluorene (92)



2,7,12-Tribromo-10,15-dihydro-5*H*-diindeno[1,2-*a*:1',2'-*c*]fluorene (**103**) (3.60 g, 6.20 mmol) in DMF (50 mL) was added over a suspension of NaH (60% in mineral oil, 0.82 g, 20.4 mmol) in anhydrous DMF (50 mL) at 0 ºC and was ultrasonicated for 50 min 1-bromo-2-(bromomethyl)naphthalene in anhydrous DMF (40 mL) was added and the mixture was stirred at r.t. overnight. Crude mixture was allowed to stand for 48 h and precipitated *syn*-isomer was filtered off and washed with CH_2Cl_2 (3 x 50 mL) to give **92** (1.46 g, 19%) as a green solid: mp > 300 ºC. ^{1}H NMR (500 MHz, $CDCl_2CDCl_2$, 130 ºC) δ 8.26 (d, J = 8.5 Hz, 3H), 7.67 (d, J = 8.1 Hz, 3H), 7.61 (d, J = 7.9 Hz, 3H), 7.54 (t, J = 7.3 Hz, 3H), 7.43 (t, J = 8.2 Hz, 3H), 7.27 (dd, J = 8.0, 1.3 Hz, 3H), 6.91 (s, 3H), 6.74 (d, J = 8.3 Hz, 3H), 4.52 (bs, 3H), 3.65 (dd, J = 13.4, 5.9 Hz, 3H), 3.20 (dd, J = 13.4, 8.3 Hz, 3H).

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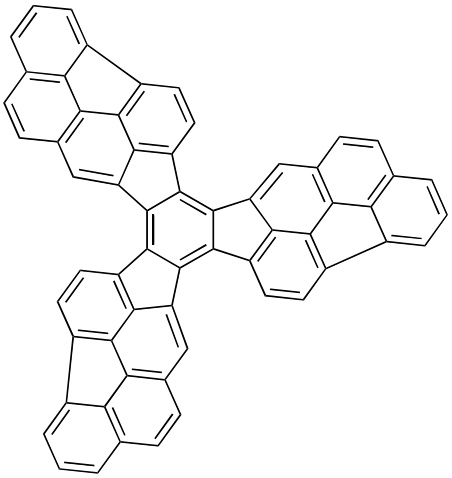
Compound $C_{60}H_{24}$ (93)



A mixture of 2,7,12-tribromo-5,10,15-tris((1-bromonaphthalen-2-yl)methyl)-10,15-dihydro-5*H*-diindeno[1,2-*a*:1',2'-*c*]fluorene (**92**) (130 mg, 0.105 mmol), $Pd(OAc)_2$ (46.1 mg, 0.21 mmol), dppe (84.5 mg, 0.21 mmol) and K_2CO_3 (220 mg, 1.54 mmol) in anhydrous DMA (1 mL) was heated at 140 ºC for 36 h. After cooling to r.t., water (10 mL) was added and the precipitated solid was filtered off and washed by centrifugation with water (2 x 50 mL), acetone (2 x 50 mL), NaCN sat. aq. (2 x 50 mL), acetone (2 x 50 mL) and CH_2Cl_2 (2 x 50 mL) to give **93** (36 mg, 47%) as a dark orange insoluble solid: mp > 300 ºC. MS-MALDI (dithranol-Ag) *m*/z 744.2 $[M]^+$.

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Chapter 2

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Chapter 2:

Design and Synthesis of Molecular Electronic Devices

1. Introduction

1.1 From Microelectronics to Molecular Electronics

As predicted by George Moore, during the last decades semiconductor-based electronic devices have been progressively shrinking in size in order to create more powerful and energetic electronic systems.[143] Noteworthy, this "up-to-bottom" approach of miniaturization that is currently being applied, is leading to few nanometers scale devices where inherent, together with technological limitations seem not feasible to overcome. Thus, a change in paradigm with a new conceptual approach must be addressed.[144] Alternatively, as Feynman had suggested,[145] molecular electronics based on the use of organic molecules capable to perform basic electronic functions, are promising for the construction of integrated circuits in a "bottom-to-up" approach. Therefore, the design, synthesis, assembly, and control of the electronic behavior of molecular systems are main challenges in nanotechnology.

1.2 Molecular Circuitries: Historical Overview

The first suggestion of potentially computing inside a single molecule was theoretically presented already in the 1970's by Aviraim and Ratner.[146] In their seminal paper, they described a molecule that could perform rectifying electronic functions. The designed molecule consisted basically on an electron-donating tetrathiafulvalene (TTF) derivative covalently linked, through a non-conjugated bridge, to an electron-accepting tetracyanoquinodimethane (TCNQ) functionalized

143 G. Moore, co-founder of Intel, observed that the number of transistor per square inch on integrated circuits doubled in size every 18-24 months. In 1965 he predicted that the trend would continue in the future; this is known as Moore's law: Moore. E. G. *Electronics*, **1965**, *38*, 114-117.

144 Whitesides, G. M.; Love, J. C. *Sci. Am*. **2001**, 38-47.

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group (*Figure 25*).

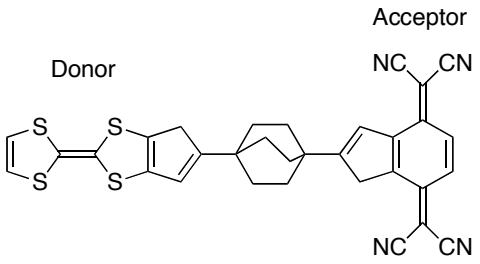

Figure 25: First proposed molecular rectifying diode.

According to their theoretical predictions, the insulating asymmetric molecule embedded between two electrodes would behave like a diode, becoming conductive after applying a certain threshold voltage that will lead to the flow of electrons from the cathode to the acceptor and then from the donor to the anode. Hence, the molecule shows rectification in terms of a strongly asymmetric flow of current. Later, in the 1980's Carter pointed out the difficulties inherent on using molecules as diodes, arguing that it will not be possible to wire millions of single molecules in order to assemble an electronic circuit in analogy to meshes and nodes used in currently fabricated inorganic solid state devices. Therefore, he suggested the integration of wires and digital functions inside a single molecule, proposing a conjugated "large" molecule with the required shape and functionalities in order to make the molecule itself to act as an integrated electronic circuit.[147] Following both envisioned ideas, the design of a wide variety of different molecular diodes, wires, switches and more complex molecular logic elements have been proposed. [148,149]

Noteworthy, using molecules instead of inorganic solid-state devices for electronics was just considered until the end of the twentieth century a futuristic conceptual idea with no experimental evidences, but, due to the intense efforts and developments, molecular electronics have now evolved from concepts to the first measurements of molecular potential circuits and comparison with quantum physics calculations. For instance, a number of techniques and molecular architectures have been developed

147 Carter, F. L. *Physica D* **1984**, *10,* 175-194.

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to study electron transport on a molecular scale. Lagmuir-Blodgett and self-assembly techniques have been employed to investigate long-range tunneling through assembled organic subunits.[150,151] Eventually, two-terminal conductance measurements of a metal-single molecule-metal junction was first reported in 1995 by using scanning tunneling microscopy (STM).[152] Later, a number of other techniques based on nanopores,[153] mechanically controlled break junctions,[154,155] electrodeposition[156] and nanolithography[157,158] have been used to investigate molecular electron transport properties. More recently, three-terminal devices, like for example field-effect transistors, have been made from carbon nanotubes[159,160] and single molecules.[161,162]

All these advances culminated in the experimental evidences of conductance through single molecules that until then where only theoretical propositions. Thus, for example, 25 years after the paper of Aviram and Ratner,[146] Metzger *et al*. proved experimentally that a monolayer of *n*-hexadecylquinolinum tricyanoquinodimethanide embedded between two aluminum electrodes present unequivocally rectifying behavior similar to conventional semiconductors by intramolecular tunneling (*Figure 26*).[163]

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150 Mann, B.; Kuhn, H. *J. Appl. Phys*. **1971**, *42*, 4398-4405.

151 Geddes, N. J.; Sambles, J. R.; Davies, D. J.; Parker, W. G.; Sandam, D. J. *Appl. Phys. Lett*. **1990**, *56*, 1916-1918.

152 Joachim, C.; Gimzewski, J. K.; Schlittler, R. R.; Chavy, C. *Phys. Rev. Lett.* **1995**,*74*, 2102-21

153 Reed, M. A.; Zhou, C.; Deshpande, M. R.; Muller, C. J.; Burgin, T. P.; Jones, L.; Tour, J. M. *Ann. N.Y. Acad. Sci*. **1998**, *852*, 133-144.

154 Reed, M. A.; Zhou, C.; Muller, C. J.; Burgin, T. P.; Tour, J. M. *Science* **1997**, *278*, 292-254.

155 Kergueris, C.; Bourgoin, J. P.; Palacin, S.; Esteve, D.; Urbina, C.; Magoga, M.; Joachim, C. *Phys. Rev. B* **1999**, *59*, 12505-12513.

156 Bezryadin, A.; Dekker, C.; Schmid, G. *Appl. Phys. Lett*. **1997**, *71*, 1273-1275.

157 Rousset, V.; Joachim, C.; Rousset, B.; Fabre, N. *J. Phys. III* **1995**, *5*, 1983-1989.

158 Di Fabrizio, E.; Grella, L.; Gentili, M.; Baciocchi, M.; Mastrogiacomo, L.; Morales, P. *Jpn. J. Appl. Phys*. **1997**, *36*, L70-L72.

159 Tans, S.; Verschueren, A. R. M.; Dekker, C. *Nature* **1998**, *393*, 49-52.

160 Misewich, J. A.; Martel, R.; Avouris, Ph.; Tsang, J. C.; Heinze, S.; Tersoff, J. *Science* **2003**, *300*, 783-786.

161 Park, H.; Park, J.; Lim, A. K. L.; Anderson, E. H.; Alivisatos, A. P.; McEuen, P. L. *Nature* **2000**, *407*, 57-60.

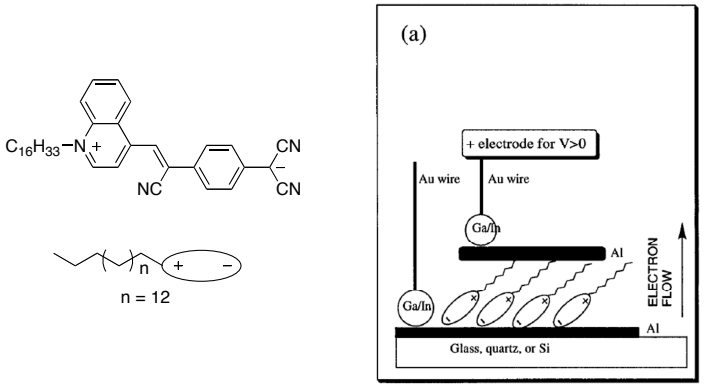

Figure 26: Monolayer of n-hexadecylquinolinum tricyanoquinodimethanide embedded between two aluminum electrodes.

In addition, Joachim and Gimzewski, developed an electromechanical amplifier device based on a C_{60} fullerene, where amplification was achieved by contacting the molecule with the STM tip which shifted and broadened the HOMO and LUMO molecular orbitals increasing the conductance through the molecule.[164] This was a proof of concept that electronic properties inherent in a single molecule can provide a variation on the conductance of the metal-molecule-metal junction device.

Besides, and having into account the meantime new experimental progresses and developments on alternative technical approaches, new conceptual theories and quantum level calculations have been maturing in order to interpret and understand the experimental results and to rationally design improved molecular devices. Shortly after the pioneering STM experimental measurements, the first molecular orbital theory of tunneling current through a molecule was developed,[165] which eventually gave raise to the Elastic Scattering Quantum Chemistry (ESQC) calculation technique in 1988.[166] This is nowadays a standard technique for calculating and interpreting STM images of molecules adsorbed on surfaces. Later,

T.; Wu, X.; Tachibana, H.; Hughes, T. V.; Sakurai, H.; Baldwin, J. W.; Hosch, C.; Cava, M. P.; Brehmer, L.; Ashwell, G. J. *J. Am. Chem. Soc.* **1997**, *119*, 10455-10466. (b) Xu, T.; Peterson, I. R.; Lakshmikantham, M. V.; Metzger, R. M. *Angew. Chem, Int. Ed.* **2001**, *40*, 1749-1752.

164 Joachim, C.; Gimzewski, J. K. *Chem. Phys. Lett.* **1997***, 265,* 353-357.

165 Joachim, C. *Chem. Phys*. **1987**, *116*, 339-349.

166 (a) Sautet, P.; Joachim, C. *Phys. Rev. B* **1988**, *38*, 12238-12247. (b) Sautet, P.; Joachim, C.

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the quantum behavior of the electron transfers process through a molecule with exponential decay as a function of its length was calculated.[167] This was followed by a large number of theoretical studies of molecular wires and switches that culminated in the possibility of theoretically design larger molecules capable of performing complex electronic functions like logic gates.

Hence, following Carter's idea, some molecular circuits have also been theoretically designed to integrate wires and logic devices inside a single molecule in order to perform more complex logic functions.[149] Significantly, three terminal devices, like transistors, are the key elements in modern electronic architectures as they allow dynamic operations like switching between currents. An elementary logic gate is generally realized by a three-branched electronic device, whose branches are connected to a common central node. In this device, two of the terminal extensions serve as channel for the input signal, whereas the third one is used for the output signal detection. As an example, Joachim and co-workers theoretically designed *OR* and *AND* molecular logic gates integrating rectifiers and wires in a large molecule as an intramolecular circuit able to perform logic functions (*Figure 27*).[168]

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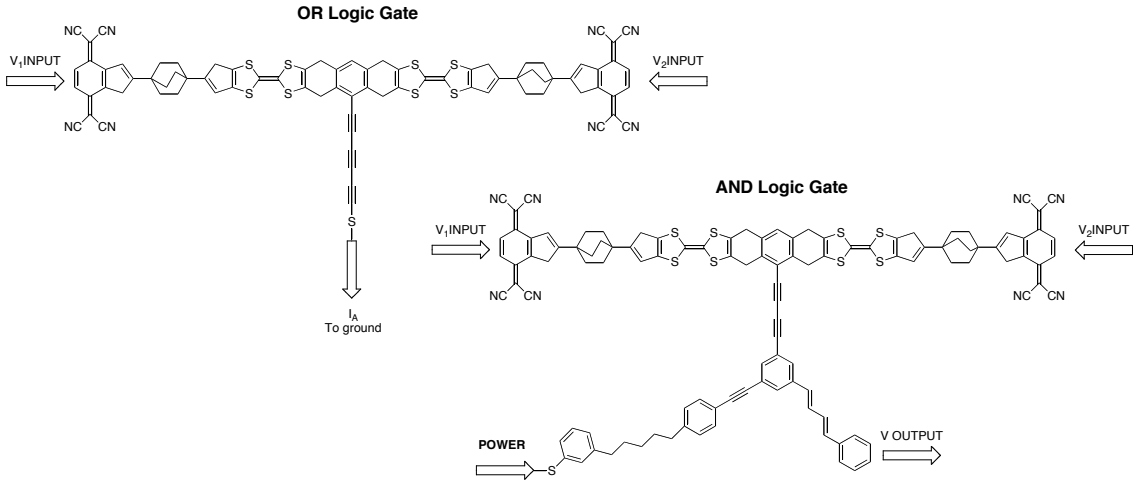

Figure 27: Molecular OR and AND logic gates integrated in a single molecule.

However, new problems appear within this approach. For instance, large molecules are not easily deposited on surfaces and, until now, they cannot be easily manipulated with the tip of the STM in order to connect them to the assigned electrodes with an accurate precision. But, more importantly, as the authors had pointed out before,[168] for intramolecular circuits, including these relatively simple molecules, the calculated electronic tunneling current intensity through the molecules is far too low (on the order of a femto-ampere), to assemble these molecular circuits in applicable electronic systems.[169] Therefore, for circuits to be built with these molecular elementary functions, the standard electronic laws for nodes and meshes on circuits, must be modified according to the quantum physics governing the electron transfer process through large molecules. Alternatively, new approaches are currently based on the interdependency between molecular electronics[148] and quantum computing.[170]

In molecular electronics, the principle of quantum computing is to take advantage of the spontaneous response of a quantum molecular system when is prepared in a non-stationary state to perform calculations. Manipulating the electronic structure of a molecule modifies its intrinsic quantum dynamics to reach a specific state while performing computation inside the molecule. The first molecular logic gate has been

169 Ami, S.; Joachim, C. *Phys. Rev. B* **2002**, *65*, 155419.

170 Nielsen, M. A.; Chiang, I. L. *Quantum Computation and Quantum Information*; Cambridge

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created by using mechanical transfer quantum information from molecule to molecule in a CO assembled molecular cascade.[171] However, this logic gate works only once, and for computing another calculation, the molecules have to be physically manipulated again. A more recent approach by Liljeroth *et al.* has been reported using intramolecular proton transfer tautomerism of a free base naphthalocyanine molecule (*Figure 28*) that induces topological rotation of the molecular orbitals and influences on the electronic states of the neighboring molecules.[172]

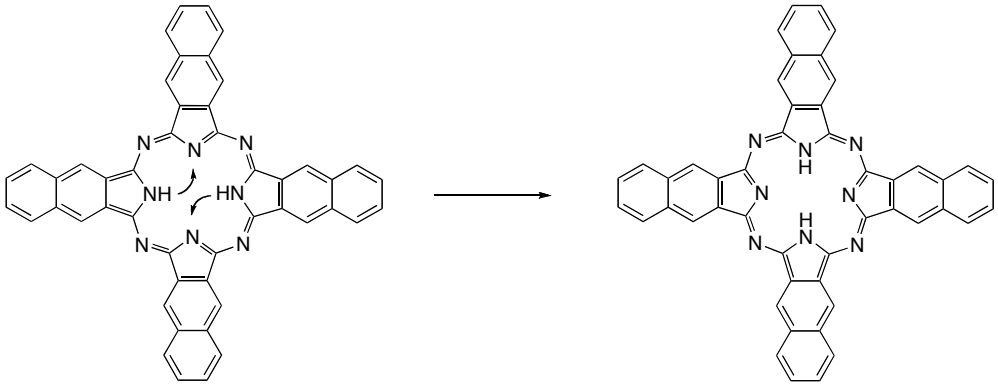

Figure 28: Proton transfer tautomerism in naphthalocyanine molecule.

All these advances are currently evolving to achieve a deeper understanding on the electronic quantum behavior that governs on molecular scale, but still more thorough studies towards the integration of complex logic functions in single molecules are required. Furthermore, new advances on technical and architecture designs have to be developed in order to multiple connect the logic molecules in real-working molecular devices.

171 Heinrich, A. J.; Lutz, C. P.; Gupta, J. A.; Eigler, D. M. *Science* **2002**, *298*, 1381-1387.

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1.3 Computing a Single Molecule: Pico-Inside Project

On the way to perform an integrated circuit where molecular logic systems can act as elemental building blocks and be interconnected with nano-scale precision, interdisciplinary collaborations between experimental and theoretical physicists together with chemists must be established in order to overcome new challenges and progresses.

Following a bottom-to-up approach, Pico-Inside interdisciplinary project[173] aimed at the design, synthesis, and application of new molecular devices for their implementation in molecular electronics. More precisely, the Pico-Inside project focused on the investigation and development of the architecture, the atomic scale technology and the chemistry, to explore the intramolecular electronic properties for integrating digital functions inside a single molecule and to multiple connect these molecules into a real-working molecular electronic devices (*Figure 29*).[174]

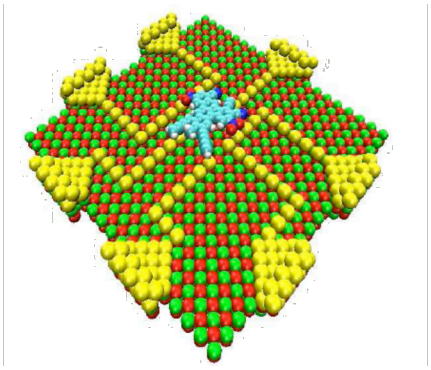

Figure 29: Pico-Inside envisioned molecular electronic device: Intramolecular Circuit Architecture.

The final molecular system that was envisioned should comprise a large circuitry molecule, fixed in a planar conformation on an insulator surface, which must be

173 Pico-Inside Integrated Project supported by the Sixth Framework Program, IST-FET (FP6-015847) and founded by the European Union, comprises fifteen groups from different disciplines included in the fields of theoretical and experimental physics and chemistry: Pico-Inside Project Partners *E-Nano* **2005**, *2*, 17-20.

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wired or connected through functional groups to several nano-electrodes (*Figure 30*).[175]

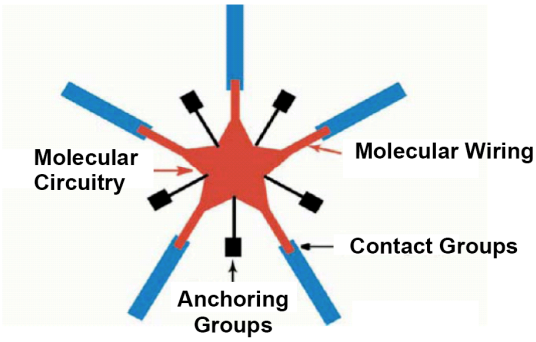

Figure 30: Pico-Inside envisioned molecular electronic device: Molecular Design.

Besides the final architectural design of complete realistic systems, preliminary studies must be carried out on simple model systems where small molecules can be deposited on an appropriate isolating surface, imaged and manipulated by means of Atomic Force Microscope (AFM) or STM, and connected to two or three electrodes in order to understand the fundamental laws governing at the nano-scale.

1.4 Molecular Circuitry Design

The design of new molecules with potential applications in material science is mainly based in the direct relation between chemical structure and properties. Structural modification on molecular scaffolds can give important variations in the physical and chemical properties of the desired applied device. Particularly, molecules that are deposited on surfaces and imaged with scanning probe techniques such as AFM and STM, require a series of specific features. For instance, molecules must adsorb to the surface, avoid diffusion, and in the case of STM imaging, must weakly interact with the tip to create a measurable tunneling current. Flat aromatic systems, such as polycyclic aromatic hydrocarbons (PAHs), are suitable for surface deposition. Non-covalent binding forces, like π-stacking[3d] and van der Waals interactions[176] allow individual molecules to be deposited on metallic surfaces,

175 Pico-Inside Project Partners, *E-Nano* **2006**, *3*, 21-30.

176 (a) Barth, J. V.; Weckesser, J.; Cai, C.; Günter, P.; Bürgi, L.; Jeandupeux, O.; Kern,

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imaged, manipulated, and when increasing molecular occupation, the controlled formation of nano-scale molecular self-assembly networks.[177] In addition, PAHs with extended π-electronic systems are suitable candidates for molecular computing since they exhibit rather small gaps between their frontier molecular orbitals promoting the electron transport.[178]

Importantly, as it was already pointed out, when thinking on a single molecule as an electronic device, the behavior of such a system at the nano-scale where quantum physics laws govern, must considered. Yet, although a complete theoretical understanding is crucial to design reproducible and controlled molecular systems, still nowadays, no calculations of electron transfer phenomenon through an entirely interconnected multi-branched molecule exist. Therefore, several classical and quantum computational approaches have been considered in the Pico-Inside project. Among them, quantum Hamiltonian computer approach (QHC) has been further developed and applied by Joachim and co-workers on two and three branched polyaromatic molecules. In the QHC approach, the molecule is prepared in a non-stationary state and its trajectory on the state space is controlled by the input status.[179,180] For instance, the change in conformation of the molecule or a functional group, will give a different quantum response after a determined input signal.[181]

For Pico-Inside project, three branched planar polyaromatic molecules were considered as model systems that could be connected or wired to two input electrodes and receive an electronically output response. According to previous studies by Joachim *et al*., for theoretically designed large logic gate molecules, (see *Figure 27*) low tunneling current is obtained in the intramolecular electron transfer

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Kamikado, T.; Okuno, Y.; Mashiko, S. *Nature* **2001**, *413*, 619-621. (c) Otero, R.; Schöck, M.; Molina, L. M.; Lœgsgaard, E.; Stensgaard, I.; Hammer, B.; Besenbacher, F. *Angew. Chem. Int. Ed*. **2005**, *44*, 2270-2275. (d) Elemans, J. A. A. W.; von Hameren, R.; Nolte, R. J. M.; Rowan, A. E. *Adv. Mater*. **2006**, *18*, 1251-1266.

177 Theobald, J. A.; Oxtoby, N. S.; Phillips, M. A.; Champness, N. R.; Beton, P. H. *Nature* **2003**, *424*, 1029-1031.

178 Bendikoz, M.; Wudl, F. *Chem. Rev*. **2004**, *104*, 4891-4945 and referentes therein.

179 Fiurasek, J.; Cerf, N. J.; Duchemin, I.; Joachim, C. *Physica E* **2004**, *24*, 161-172.

180 Duchemin, I.; Joachim, C. *Chem. Phys. Lett*. **2005**, *406*, 167-172.

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process.[168,169] Therefore, simple and smaller molecules, with lower electron current decay, must be synthesized and experimentally studied. For Pico-Inside purposes, we centered our efforts in two classes of three branched polyaromatic molecules: non-alternant heptacyclic truxenes and cata-condensed three linear fused Y-shaped molecules like straphenes.

Polyaromatic truxene derivatives,[182,183] and more recently electron rich azatruxene analogues,[184] have already been designed for their application in organic electronics and their charge transport properties have been evaluated.

One of the main difficulties with planar aromatic hydrocarbons is to immobilize them on non-metallic surfaces. The high mobility of organic molecules on perfect insulating surfaces requires the addition of anchoring groups to the flat aromatic backbone in order to maintain the molecule fixed to the surface (*Figure 31*).

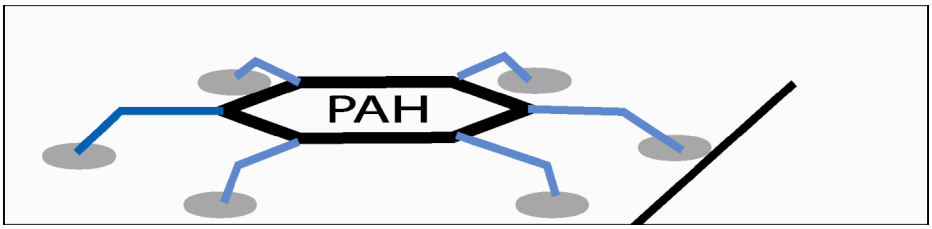

Figure 31: Schematic view of PAH with anchoring groups on surface deposition.

Due to their structural and conformational properties, truxene and readily functionalized truxene derivatives are attractive polyaromatic three-branched model systems towards intramolecular computing studies. Truxenes provide a unique platform for the preparation of C_3-symmetric *syn*-polyaromatic tripods with an

182 (a) Sun, Y.; Xiao, K.; Liu, Y.; Wang, J.; Pei, J.; Zhu, D. *Adv. Funct. Mater.* **2005**, *15*, 818-822. (b) Wang, J. -L.; Yan, J.; Tang, Z. -M.; Xiao, Q.; Ma, Y.; Pei, J. *J. Am. Chem. Soc.* **2008**, *130*, 9952-9962. (c) Wang, J. -L.; Tang, Z. -M.; Xiao, Q.; Zhou, Q.-F.; Ma, Y.; Pei, J. *Org. Lett.* **2008**, *10*, 7-20.

183 Sanguinet, L.; Williams, J. C.; Yang, Z.; Twieg, R. J.; Mao, G.; Singer, K. D.; Wiggers, G.; Petschek, R. G. *Chem. Mater.* **2006**, *18*, 4259-4269.

184 García-Frutos, E. M.; Gutierrez-Puebla, E.; Monge, M. A.; Ramírez, R.; de Andrés, P.; de

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almost flat aromatic core and three groups extending above the surface.[185] Thereby, three aromatic pendant groups could serve as legs for anchoring while maintaining the aromatic core detached from the surface, acting as small molecular landers (*Figure 32*).[176c]

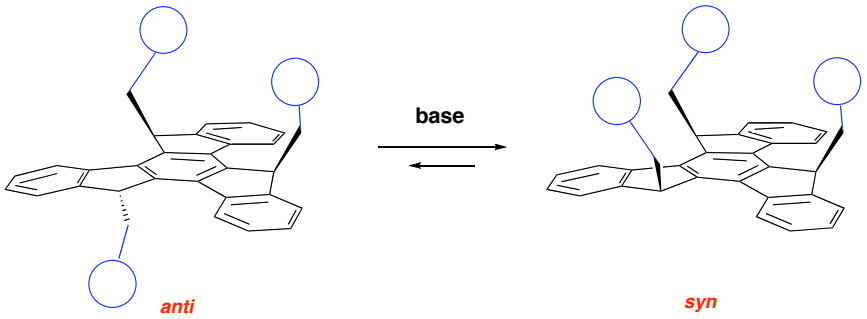

Figure 32: Base-catalyzed isomerization of 5,10,15-trisubstituted truxene.

The second family of molecules that have been considered by Pico-Inside partners are fully conjugated Y-shaped molecules like starphenes, where three branches of benzenoid rings are annellated to a central benzene ring. This type of molecules may be seen as simple molecular wires where π-extended conjugation will permit a sufficient electron tunneling current for measuring a computation (*Figure 33*). According to theoretical calculations, during the electron transmission process, the tunneling current decay exponentially with the increase of the wire length. The synthesis and preparation of different length branched molecules would allow to experimentally study the current dependence in these molecular wires.[186]

185 (a) de Frutos, Ó.; Gómez-Lor, B.; Granier, T.; Monge, M. Á.; Gutiérrez-Puebla, E.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **1999**, *38*, 204-207. (b) Gómez-Lor, B.; de Frutos, Ó.; Ceballos, P. A.; Granier, T.; Echavarren, A. M. *Eur. J. Org. Chem.* **2001**, 2107-2114. (c) Gómez-Lor, B.; González-Cantalapiedra, E.; Ruiz, M.; de Frutos, Ó.; Cárdenas, D. J.; Santos, A.; Echavarren, A. M. *Chem. Eur. J.* **2004**, *10*, 2601-2608.

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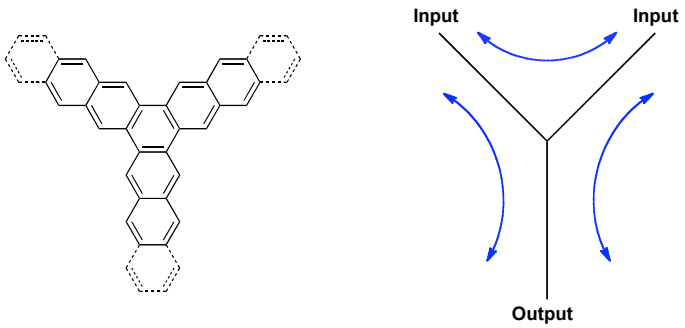

Figure 33: Starphene molecular wire.

Moreover, by chemically tuning the nature of one or two of the branches, for instance by introducing heteroatoms or by breaking the conjugation with saturated rings, could mimic conventional classic logic gates, just as suggested by Carter, but considering much smaller molecular systems than before.[186]

In a standard electrical circuit, logic functions are achieved when elemental functions are incorporated in some of the branches making them electronically and topologically different. For instance, in an *OR* logic gate, two rectifiers are required to avoid any direct current from one input to the other. Considering the tunneling current decay through a molecular wire, a way to isolate the two inputs in a three-branched molecular device is to play with this exponential decay, which must be much faster between the two inputs than between one input and the output.

Theoretical studies by Pico-Inside partners have shown that an *OR* logic gate molecule built by assembling two Ratner-Aviram diodes in two of the three branches, delivers a too small output current intensity to be used as elemental molecular logic device. Nevertheless, according to calculations, by reducing the molecular diode length, or by changing the intrinsic electronic structure of the branches, molecular logic gate could be potentially redesigned like shown in *Figure 34*.[186]

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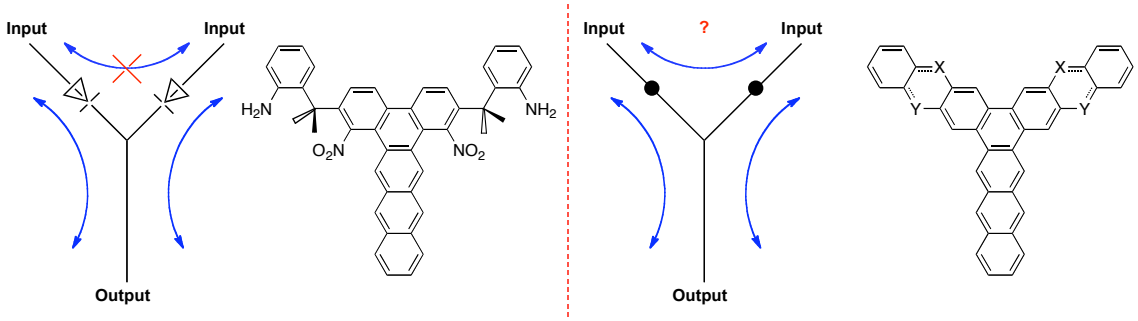

Figure 34: (a) Classical OR-logic gate with two rectifiers, (b) redesigned system in which the exponential decay of the conductance of the molecule is used to obtain the same OR functionality but without rectifying chemical groups.

In order to interconnect the branched molecules with the metallic electrodes, several approaches have been theoretically considered and experimentally explored. For instance, the terminal branches could be directly in contact with the metallic electrode pads, or alternatively, the molecule could be deposited on the insulating layer and connected to the electronic pads through molecular wires (*Figure 35*).

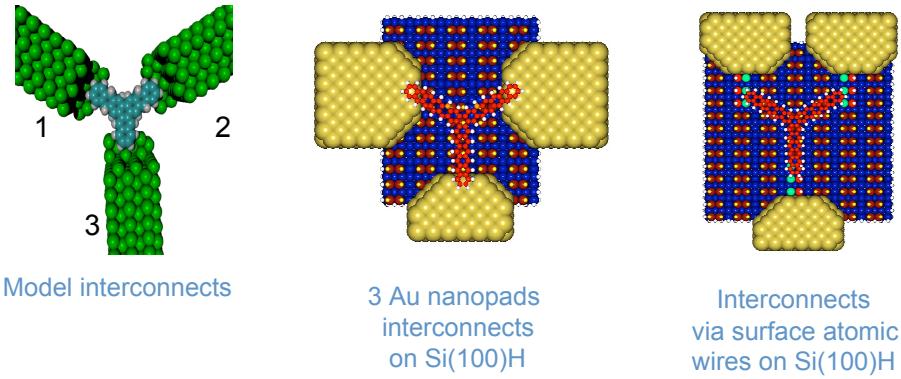

Figure 35: Approaches to interconnect starphenes with gold nano-electrodes.

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2. Objectives

Taking into account the state-of-the-art in molecular electronics, the main objective of the Pico-Inside project was to explore the laws that govern in the nano-scale in order to achieve new progresses and developments on single molecule devices for proposing new theories, technological solutions, and designs for future applications.

Our contribution to the project was the design and synthesis of new polyaromatic scaffolds for their application as molecular circuitries. Considering the precedents on the computational design of large logic gates molecules and our main interest in understanding the fundamental laws that govern at the molecular scale, we focused our work in three branched simple model systems like truxenes and starphenes.

The ready functionalization of truxenes could allow us to incorporate different substituents as anchoring groups and to study the best conditions for attaching these type of molecules on different insulating surfaces. The first functional groups that we planned to study will be based in flexible benzyl and larger pendant aryl moieties like anthracene or benzanthracene that could efficiently anchor to the surface. Addition of heteroatoms, like nitrogen or oxygen, on the aryl rings may also be needed to fix the truxene depending on the insulating substrate and on the scanning probe measurements that will be experimentally employed.

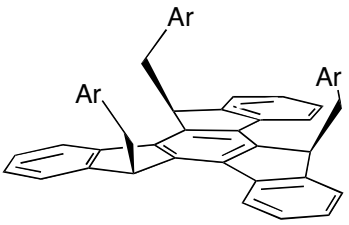

Figure 36: 3D representation of triaryl syn-substituted truxene.

We also planned the synthesis of a wide range of polyaromatic Y-shaped molecules, like starphenes with extended aromatic branches. In the first place, the synthesis of fully aromatic starphenes without functional groups would allow us to experimentally study the π-conjugation on three branched aromatic systems, and the dependence of the aromatic ring extension on the electronic transfer process when

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saturated bonds in some or all of the branches to study the influence on the electron transport process.

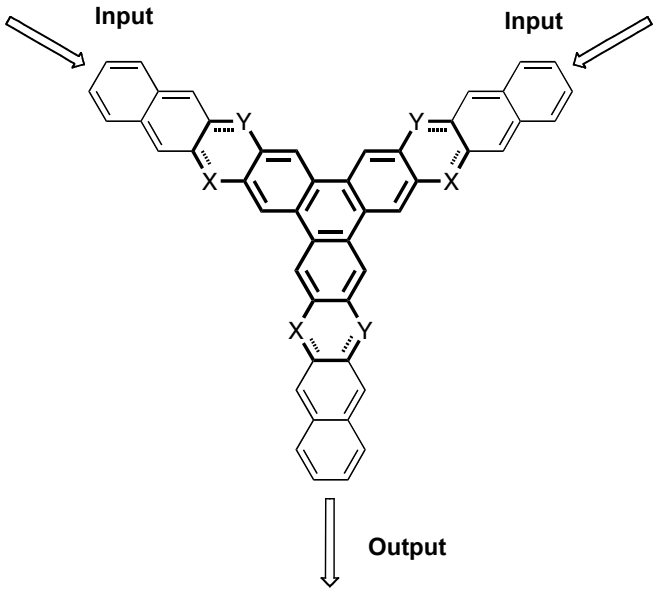

Figure 37: Starphene derivatives as simple molecular wires.

In contrast to the well-known procedure for the functionalization of truxenes,[185] less is know on the synthesis and functionalization of large starphenes. Therefore, a new challenge in the present work was to explore different divergent approaches for the construction of large fully aromatic starphenes and non-aromatic starphene derivatives.

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3. Results and Discussion

3.1 Synthesis of Truxenes[187]

The heptacyclic polyarene truxene (10,15-dihydro-5*H*-diindene[1,2-*a*;1',2'-c]fluorene) **1**,[188] is a planar non-alternant PAH that has attracted attention as potential starting materials for the construction of large polyarenes[185,189] and for the synthesis of new materials.[190,191,192,193]

Truxene based tripods with C_3-symmetry can be readily prepared by a deprotonation/alkylation sequence followed by base promoted isomerization, which leads exclusively to trisubstituted *syn*-isomers with a planar aromatic core and three pendant groups standing above the surface (*Scheme 51*).[185] Following this procedure, we have prepared a series of *syn*-substituted truxenes.

187 Part of the work on the synthesis of truxenes was carried out in collaboration with Dr. Catelijne H. M. Amijs.

188 Dehmlow, E. V.; Kelle, T. *Synth. Commun.* **1997**, *27*, 2021-2031.

189 Pascual, S.; de Mendoza, P.; Echavarren, A. M. *Org. Biol. Chem.* **2007**, *5*, 2727-2734.

190 Gómez-Lor, B.; Echavarren, A. M. *Org. Lett.* **2004**, *6*, 2993-2996.

191 (a) Perova, T. S.; Vij, J. K. *Adv. Mater.* **1995**, *7*, 919-922. (b) Fontes, E.; Heiney, P. A.; Ohba, M.; Haseltine, J. N.; Smith, A. B. *Phys Rev. A* **1988**, *37*, 1329-1334. (c) Warnerdam, T.; Nolte, R. J. M.; Drenth, W.; van Miltenburg, J. C.; Frenkel, D.; Ziljlstra, R. J. J. *Liq. Cryst.* **1988**, *3*, 1087-1104. (d) Destrade, C.; Malthete, J.; Tinh, N. H.; Gasparoux, H. *Phys. Lett.* **1980**, *78A*, 82-84.

192 Jacob, K.; Becker, J. Y.; Ellern, A.; Khodorkovsky, V. *Tetrahedron Lett.* **1999**, *40*, 8625-8628.

193 (a) Pei, J.; Wang, J.-L.; Cao, X.-Y.; Zhou, X.-Y.; Zhang, W.-H. *J. Am. Chem. Soc.* **2003**, *125*, 9944-9945. (b) Cao, X.-Y.; Zhang, W.-B.; Wang, J.-L.; Zhou, X.-H.; Lu, H.; Pei, J. *J. Am. Chem. Soc.* **2003**, *125*, 12430-12431. (c) Cao, X.-Y.; Liu, X.-H.; Zhou, X.-H; Zang, Y.; Jiang, Y.; Cao, Y.; Cui, Y.-X.; Pei, J. *J. Org. Chem.* **2004**, *69*, 6050-6058. (d) Kanibolotsky, A. L.; Berridge, R.; Skabara, P. J.; Perepichka, I. F.; Bradley, D. D. C.; Koeberg, M. *J. Am.*

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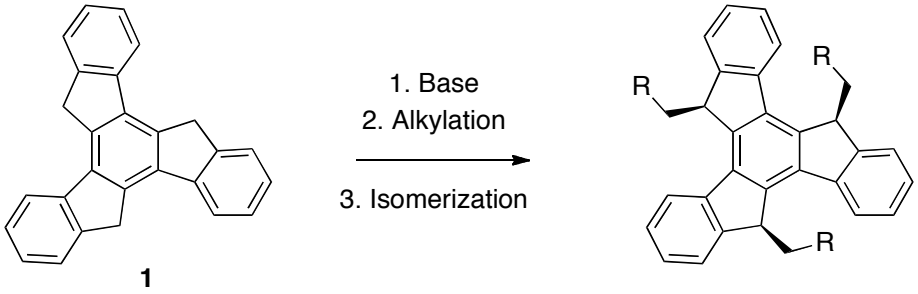
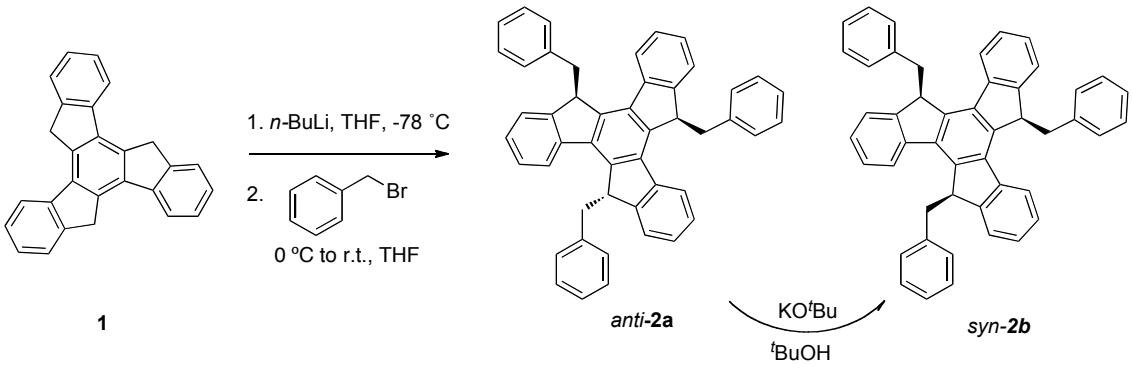


Scheme 51

3.1.1 Synthesis of *syn*-Tribenzyltruxene

syn-5,10,15-Tribenzyltruxene **2b** (*Scheme 52*) was initially considered as a model system to understand the quantum behavior inside this family of non-alternant aromatic compounds and to analyze the experimental results upon deposition and imaging of the truxenes derivatives on insulating surfaces.

Functionalized truxene **2b** was synthesized according to the standard procedure developed previously in our group.[185] Starting with truxene **1**, deprotonation with 3 equiv of *n*-BuLi and alkylation with bromobenzylbromide afforded the anti/syn (*ca*. 3:1) mixture of tribenzyltruxenes **2**. Isomerization with *t*-BuOK in *t*-BuOH yielded the corresponding *syn*-isomer **2b** (*Scheme 52*).



Scheme 52

syn-Tribenzyltruxene **2b** was deposited on a NaCl insulating surface, imaged at low temperature, and manipulated by means of STM under UHV conditions (see section 4.1).[194]

194 Christian Joachim's research group at the CMES/CNRS: *Centre d'Elaboration des*

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As mentioned, in contrast to STM experiments of PAHs deposited on metallic surfaces where aromatic boards provide sufficient anchoring to fix the molecules,[195] insulating surfaces exhibit much weaker interaction with polyaromatic molecules. Thus, the high mobility of *syn*-benzyltruxene and its conformational freedom, presented some difficulties to control the single molecule surface anchoring, therefore, we considered the introduction of larger polyaromatic pendant groups and the addition of polar functional groups in the aryl rings that could interact stronger with the surface.

3.1.2 *syn*-Cyanobenzyltruxene

It has been reported that cyano groups, which have a large dipole moment, incorporated in aromatic systems such as porphyrins, act as anchoring groups when deposited on KBr surfaces.[196]

To fix single truxene molecules on insulating surfaces at room temperature, we prepared two differently substituted *syn*-cyanobenzyl truxenes: *syn*-5,10,15-tris-(4-cyanophenylmethyl)truxene (**3a**) and *syn*-5,10,15-tris-(3-cyanophenylmethyl) truxene (**3b**) containing three flexible benzonitrile substituents that could anchor to the surface. Both molecules were synthesized as previously reported in our group,[185] by alkylation/isomerization of truxene **1** with 3-(bromomethyl)benzonitrile and 4-(bromomethyl)benzonitrile, respectively.

195 Rosei, F.; Schunack, M.; Jiang, P.; Gourdon, A.; Lægsgaard, E.; Stensgaard, I.; Joachim, C.; Besenbacher, F. *Science* **2002**, *296*, 328-331.

196 Maier, S.; Fendt, L-A.; Zimmerli, L.; Glatzel, T.; Pfeiffer, O.; Diederich, F.; Meyer, E.

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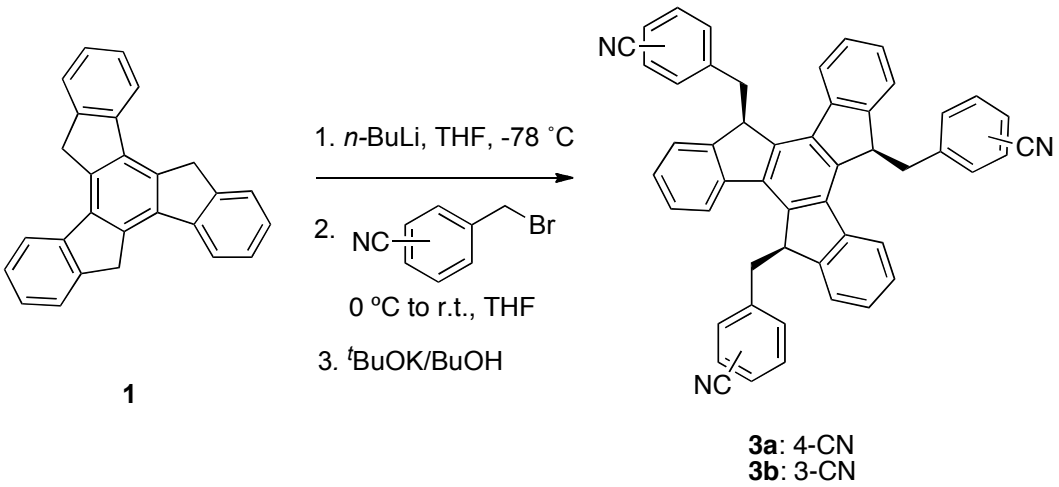

Scheme 53

Cyanobenzyl truxenes **3a** was deposited on a KBr surface and AFM imaged at room temperature[197] (see section 4.2).

3.1.3 Synthesis of *syn*-Tris(benzanthracenylmethyl)truxene

To immobilize the truxene with larger polyaromatic pendant group, we decided to introduce benz[*a*]anthracene as anchoring group. The alkylating agent, 5-(bromomethyl)benz[*a*]anthracene (**7**) was synthesized in five steps (*Scheme 54*) following the described procedure for the synthesis of 3-methyl-l,2-benzanthracene (**6**),[198] and subsequent radical bromination. The first step involved a Friedel-Crafts acylation with methylnaphthalene and phthalic anhydride to give benzophenone **4**. Selective reduction of **4** in the presence of Zn and base led to benzoic acid **5**. Ring closure of compound **5**, through a condensation in neat sulfuric acid, followed by reduction/aromatization processes using zinc and a base yielded **6**.[198] Finally, standard radical bromination[199] furnished desired compound **7**.

197 Ernst Meyer's research group at the *Insitute of Physics*, University of Basel, Switzerland.

198 Newman, M. S.; Gaertner, R. *J. Am. Chem. Soc.* **1950**, *72*, 264-273.

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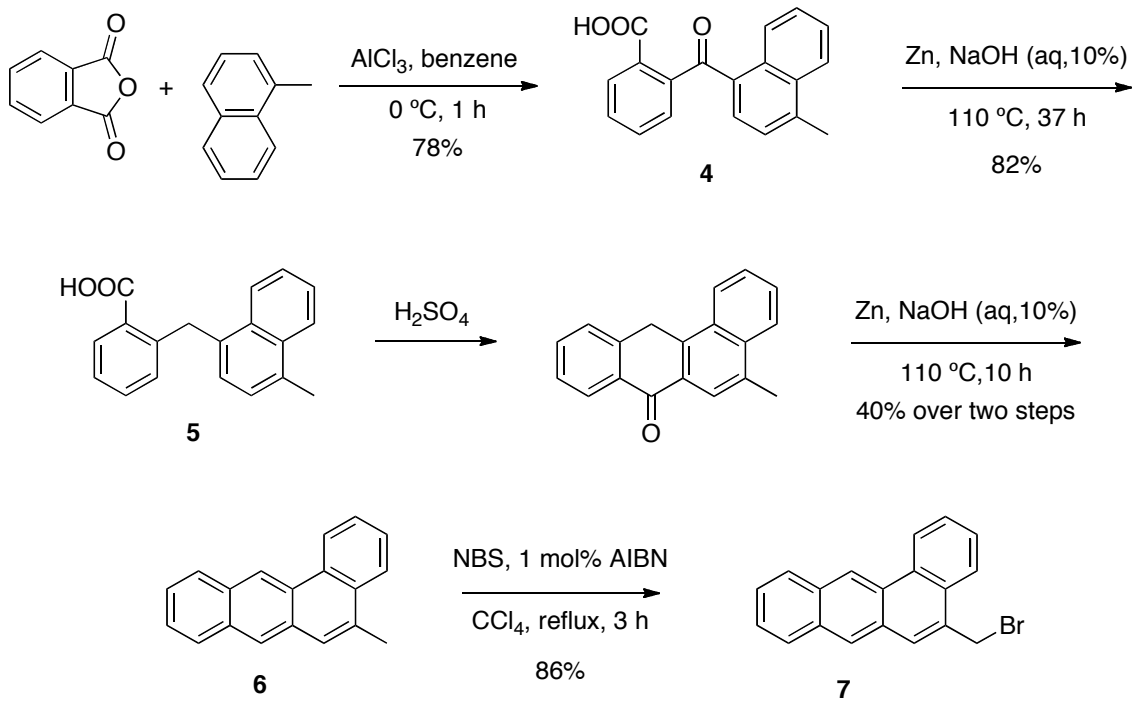
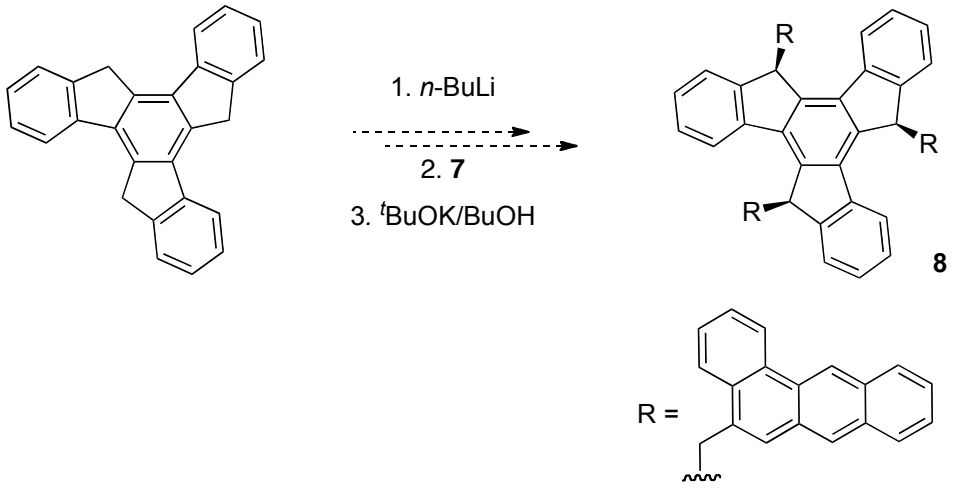


Scheme 54

Alkylation of truxene **1** with compound **7** and later isomerization to prepare *syn*-**8** was essayed under the reported conditions in our group.[185] Unfortunately, due to the probable high insolubility of the resulting alkylated truxene and to the steric hindrance of the bulky aryl moieties, mixtures of isomers and by-products were obtained from which *syn*-**8** isomer could not be isolated in a pure form.



Scheme 55

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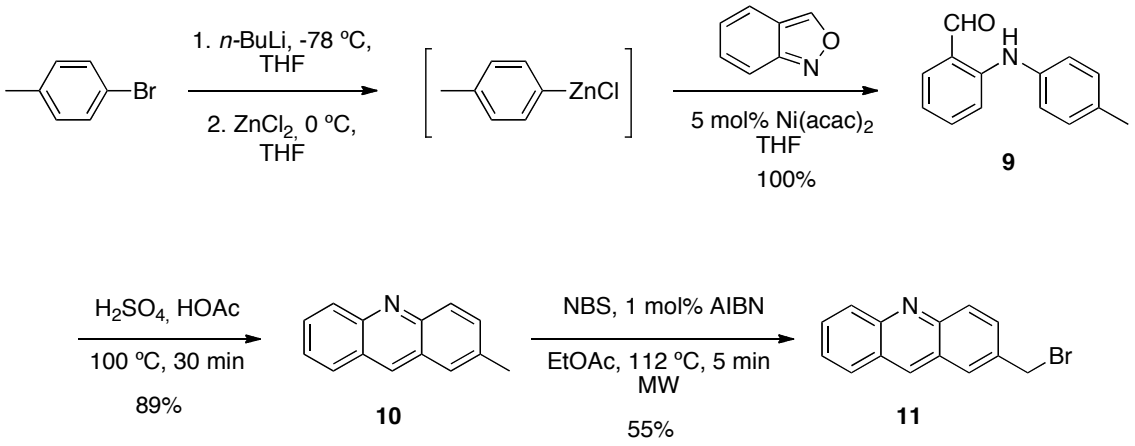
3.1.4 Synthesis of *syn*-Tris(acridin-2-ylmethyl)truxene

To reduce insolubility and isomerization difficulties, we chose acridine as an alternative aromatic substituents that should present less steric hindrance than benzanthracenylmethyl **6**, facilitating the isomerization step. Thus, the presence of nitrogen atoms on the aromatic core should increase the solubility of the final truxene and could serve to attach stronger to the surface.

The electrophilic alkylating agent **11** was synthesized in a four-step procedure starting from 4-bromotoluene (*Scheme 56*). The first step involved a nickel-catalyzed *N*-aryl coupling between tolylzinc chloride and anthranyl according to a described procedure.[200] The product **9** was subsequently heated with acid[201] after which a benzylic bromination was carried out under microwave irradiation[202] to yield **11**.



Scheme 56

Alkylation of truxene **1** with **11** and subsequent isomerization yielded **12b** in 71% yield.

200 Baum, J. S.; Condon, M. E.; Shook, D. A. *J. Org. Chem.* **1987**, *52*, 2983-2988.

201 Kitahara, Y.; Mizuno, T.; Kubo, A. *Tetrahedron* **2004**, *60*, 4283-4288.

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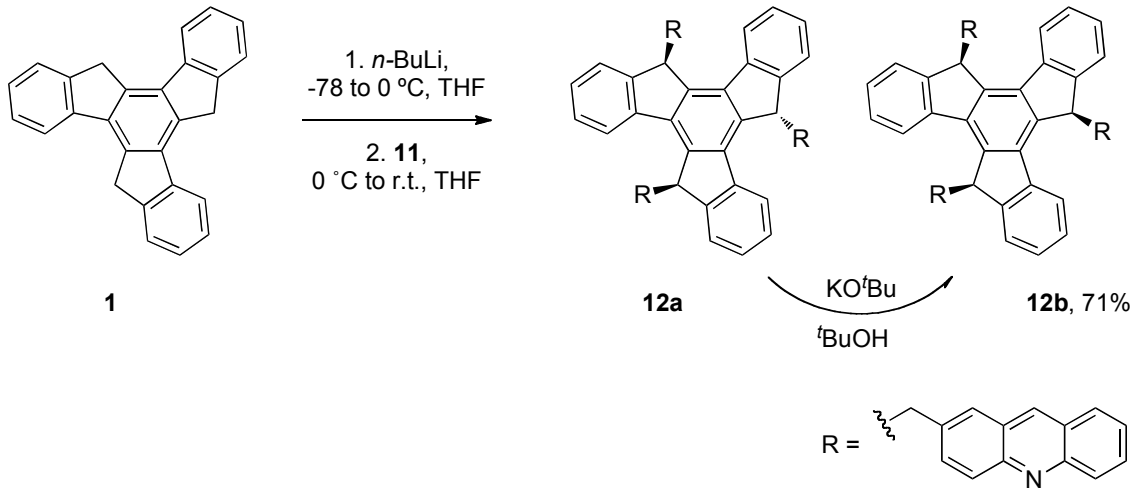

Scheme 57

Compound **12b** was preliminary analyzed by the group of Meyer[197] for the analysis of the deposited molecule on insulated surfaces (NaCl, KBr) by NC-AFM. However, until now, not conclusive results have be obtained.

3.2 Synthesis of Y-Shaped Molecules

3.2.1 Demands on Y-shaped Molecules as Logic Gates

Following our objective on the synthesis of polyaromatic molecules mimicking three terminal logic gate devices, we aimed to prepare π-conjugated Y-shaped molecules with naphthalene, anthracene, or even higher acenes branches.

Starphenes are three branched conjugated benzenoid rings annellated to alternate bonds of a central benzene ring, radiating linearly to it (a few examples are depicted in *Figure 38*).[203]

203 Clar and Mullen first proposed the nomenclature for starphenes, following the principle introduced by T. H. Goodwin and D. A. Morton-Blake where the number of aromatic rings from each branch is specify in the brackets and the total number of rings are included in the name of the starphene. See: (a) Clar, E.; Mullen, A. *Tetrahedron* **1968**, *24*, 6719-6724. (b)

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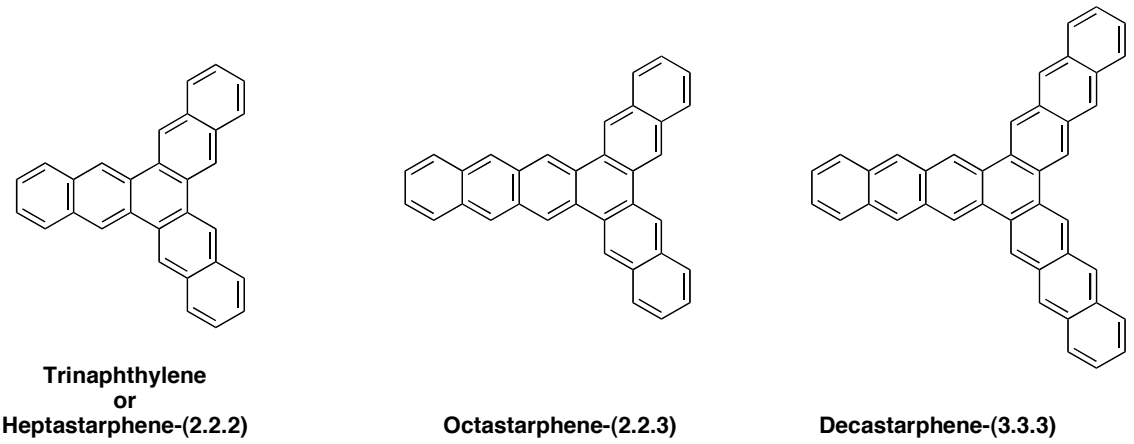

Figure 38: Representative starphenes.

According to the work of Clar *et al.* with a variety of starphenes, the UV and visible spectra indicate that the aromatic conjugation involves only two branches of the molecule, while the third branch is isolated from the π-electron delocalized system of the other two branches as represented in *Figure 39*.[204,205]

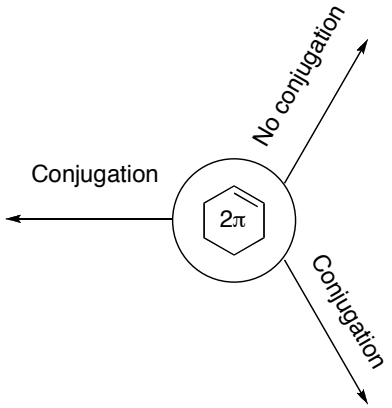

Figure 39: Aromatic conjugation on starphene derivatives

This feature makes C_3 fully symmetric starphenes interesting candidates for studying their behavior on the molecular scale when subjected them to quantum currents. Thus, starphenes are already systems with dynamic electronic properties that may serve as logic devices while measuring the tunneling electron current through the branches connected to the electrodes. Important alterations on the starphenes can be

204 Clar, E.; McCallum. A.; Robertson, R. A. *Tetrahedron* **1962**, *18*, 1471-1475.

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obtained by substituting CH-units with heteroatoms. In particular, the presence of nitrogen atoms in the structure could not only have a significant influence on the molecular electronic properties but may also facilitate their deposition and anchoring on insulating surfaces.

Besides, C_3-symmetric starphenes, another class of three branched aromatic compounds are helicenes such as benzo[*c*]naphtho[1,2-*f*]tetraphene (see *Figure 40*) and its higher homologues. Although structurally related to starphenes, having as main feature three aromatic branches that could be connected to the electrodes, the different ramification present in helicenes may have considerably effects on their static and their dynamic electronic properties. Thus, helicenes with appropriate substituents have also been considered in Pico-Inside for acting as molecular circuitry and/or molecular wires to interconnect the molecules with the electrodes.[206]

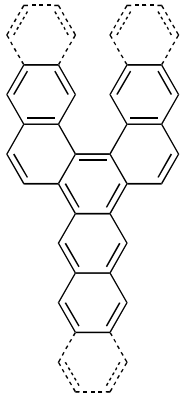

Figure 40: Representation of benzo[c]naphtho[1,2-f]tetraphene and higher Y-shaped homologues.

Moreover, apart from fully unsaturated three branched aromatic systems, those with a break in their conjugation have been predicted to perform electronic logic functions when applying quantum electronic currents.[186] The nature of the break, which can be fine-tuned by chemical methods, may lead to important changes on the intrinsic

206 Sehnal, P.; Stará, I. G.; Saman, D.; Tichy M.; Mísek, J.; Cvacka, J.; Rulísek, L.; Chocholousová, J.; Vacek, J.; Goryl, G.; Szymonski, M.; Císarová, I.; Stary, I. *Proc. Natl.*

electronic properties of the molecular device. According to the theoretical calculations based on the intramolecular electron current decay, we designed a Y-shaped molecule with two xanthene branches (*Figure 41*) as a suitable molecule that could act as an *OR* logic gate when embedded between electrodes.

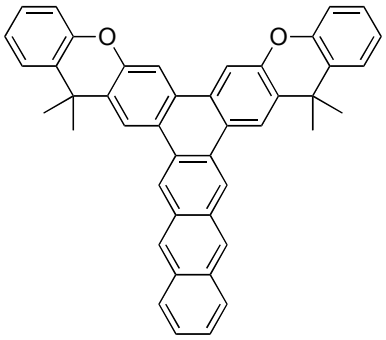

Figure 41: Theoretical and chemical designed Y-shaped OR molecule.

3.2.2 General Strategies for the Synthesis of Triphenylenes and Azatriphenylenes

Although chemical and physical properties of starphenes have been theoretically studied and a wide variety of triphenylenes, like unsubstituted triphenylene **13**, have been previously prepared, due to the difficulties in their synthesis, isolation, and characterization, less has been investigated for the construction of larger Y-shaped molecules. Therefore, new divergent approaches that allow for the preparation of a wider family of starphenes must be explored.

Triphenylene derivatives tend to self-assemble to form discotic liquid crystals. On account of their photoconductivity and high charge carrier mobility, triphenylene-based columnar discotic liquid crystals show great potential as molecular organic materials for optoelectronic devices.[207] Diverse strategies have been developed for their synthesis based on the preparation of key intermediates (*Scheme 58*).[208]

207 Kumar, S. *Liq. Crys*. **2005**, *32*, 1089-1113 and referentes therein.

208 (a) Buess, C. M. Lawson, D. D. *Chem Rev*. **1960**, *60*. 313-330. (b) Pérez, D.; Guitián, E.

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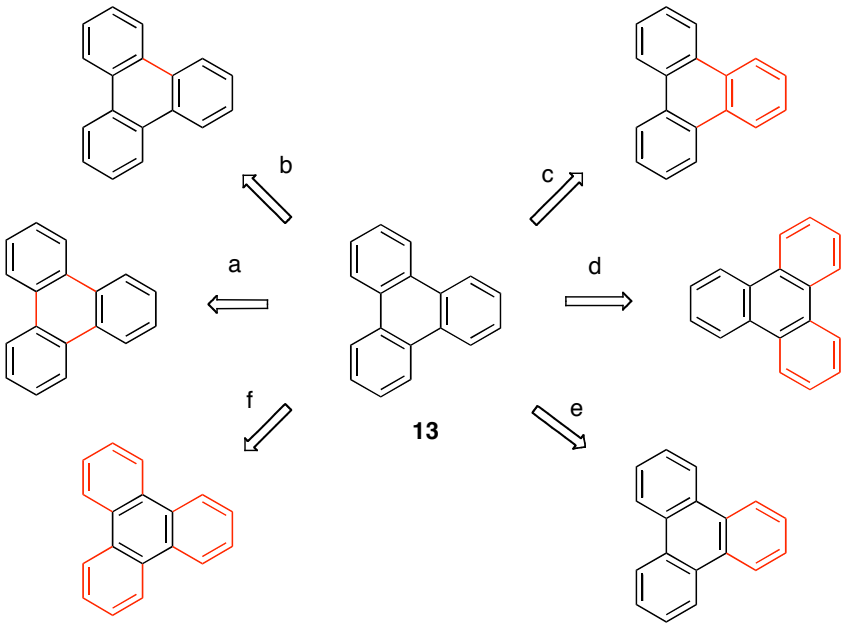

Scheme 58

Trimerization of phenyl (*strategy a*) or cyclization of *ortho*-terphenyl (*strategy b*) have been applied as the final key steps for the synthesis of triphenylenes. Functionalized biphenyls, naphthalenes, or phenanthrenes (*strategies c, d and e*) have also been reported as precursors for the formation of substituted and π-extended triphenylenes. Finally, fully (or highly) functionalized benzenes have served as the main core for building up fully symmetric triphenylenes (*strategy f*).

Metal catalyzed trimerization of arynes has been used as a direct straightforward methodology for the synthesis of triphenylenes.[209] In general, photochemical[210,211] or Lewis acid promoted oxidative cyclizations[212,213] have been used for the closure of *ortho*-terphenyl precursors that can be prepared traditionally by Ullman reaction or, recently more frequently employed, by palladium-catalyzed cross-coupling reaction. Besides, Diels-Alder cycloaddition have been extensively applied as the key step when using biphenyls, naphthalenes or phenanthrenes for the preparation of cyclized adducts that after further steps (elimination or retro Diels-Alder) result in the desired

209 Zhou, Z. H.; Yamamoto, T. *J. Organomet. Chem.* **1991**, *414*, 119-127.
210 Sato, T.; Shimada, S.; Hata, K. *Bull. Chem. Soc. Jpn*. **1971**, *44*, 2484-2490.
211 Bushby, R. J.; Hardy, C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 721-723.
212 Borner, R. C.; Jackson, R. F. W. *J. Chem. Soc., Chem. Commun.* **1994**, 845-846.

triphenylene products.[214,215] Furthermore, the Friedel-Crafts-like reaction has also been used with naphthalene functionalized precursors,[216] while condensation of 9,10-phenanthrenedione with cyano compounds furnish functionalized π-extended triphenylenes.[217] Moreover, preparation of azatriphenylenes has also been reported *via* condensation of hexaaminobenzene with 1,2-dicarbonyl derivatives[218] or condensation of hexaketocyclohexane with 1,2-diamino derivatives.[219]

3.2.3 General Strategies for the Synthesis of Extended Acene Branches

Besides the precedent methodologies employed for the synthesis of triphenylenes, we also needed to consider the possible strategies for preparing homologues with larger acene branches. Naphthalene, anthracene, or higher acene derivatives could be used as key precursors before applying one of the strategies just presented for the preparation of triphenylenes. Whereas, on the other hand, acene branches could be extended by homologation/annelation reported processes after the preparation of the central aromatic triphenylene core. Importantly, when more than one specific target molecule is aimed, divergent synthetically approaches that can give access to several homologues are favored compared to linear approaches which lead to a single target molecule.

Crucial aspects for synthetic chemistry are accessibility, stability, and solubility properties in order to warrant a reliable access to the desired structures. A general approach for the synthesis of pentacenes and higher acene derivatives is the use of quinone analogues because they are more stable than simple acenes, which are especially sensitive to oxidations. Moreover, quinones can be easily functionalized with anchoring groups, like alkynyl, aryl or alkyl chains, or simply be reduced in the

214 Raymo, F. M.; Parisi, M. F.; Kohnke, F. H. *Tetrahedron Lett*. **1993**, *34*, 5331-5332.

215 Hart, H.; Lai, C. Y.; Nwokogu, G. C.; Shamoulian, S. *Tetrahedron* **1987**, *43*, 5203-5224.

216 Rahman, A. U.; Tombesi, O. L. *Chem. Ber*. **1966**, *99*, 1805-1809.

217 Yang, C.; Yang, D.; Harvey, R. G. *Synlett* **1992**, 799-800.

218 (a) Kohne, B.; Praefcke, K. *Leibigs Ann. Chem*. **1985**, 522-28. (b**)** Rogers, D. Z. *J. Org. Chem*. **1986**, *51*, 3904-3905.

219 (a) Kanakarajan, K.; Czarnik, A. W. *J. Org. Chem*. **1986**, *51*, 5241-5243. (b) Rademacher, J.

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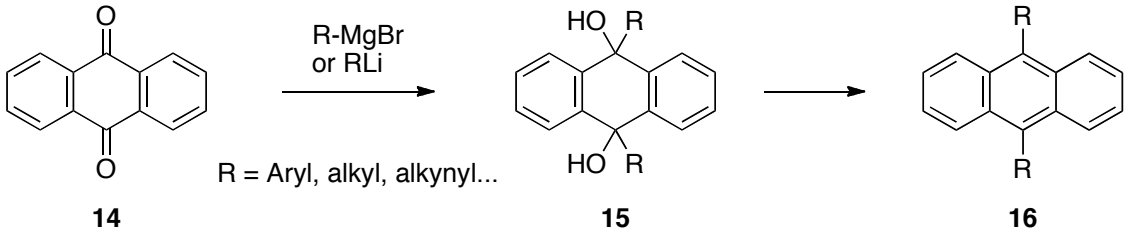
final step to obtain the unsubstituted acene. For example, diaryl[220] or dialkynyl[221] substituted acenes, respectively, are usually prepared from quinones (like **14**) and the corresponding organometallic Grignard or lithium reagents to give diols (**15**). Dehydroxylation with reducing agents in acid media affords the substituted acenes (**16**) as shown in *Scheme 59*. Importantly, certain substituents could act as anchoring or connecting groups in our final molecular circuitry design.



Scheme 59

One of the standard methods employed for the reduction of quinones is the use of aluminum-amalgam.[222] Alternative, to avoid the use of environmental deleterious mercury, Clemmensen reduction with Zn in the presence of base or, with metal hydrides like $NaBH_4$ and $LiAlH_4$, have also been frequently employed. In particular, the mechanism proceeding in the reduction of pentacenequinone (**17**) to pentacene (**18**) when using $LiAlH_4$, have been studied in detail.[223] Based on the identification of isolated or NMR detected intermediates, they showed that reduction occurs in a four-step sequence through alcohol intermediates, followed by dehydration promoted by treatment with HCl (*Scheme 60*).

220 Allen, C. F. H.; Bell. A. *J. Am. Chem. Soc*. **1942**, *64*, 1253-1260.

221 Maulding, D. R.; Roberts, B. G. *J. Org. Chem*. **1969**, *34*, 1734-1736.

222 Bruckner, V.; Karczag. W. A.; Kormendy, K.; Meszaros, M.; Tomasz, J. L. *Tetrahedron Lett.* **1960**, *1*, 5-6.

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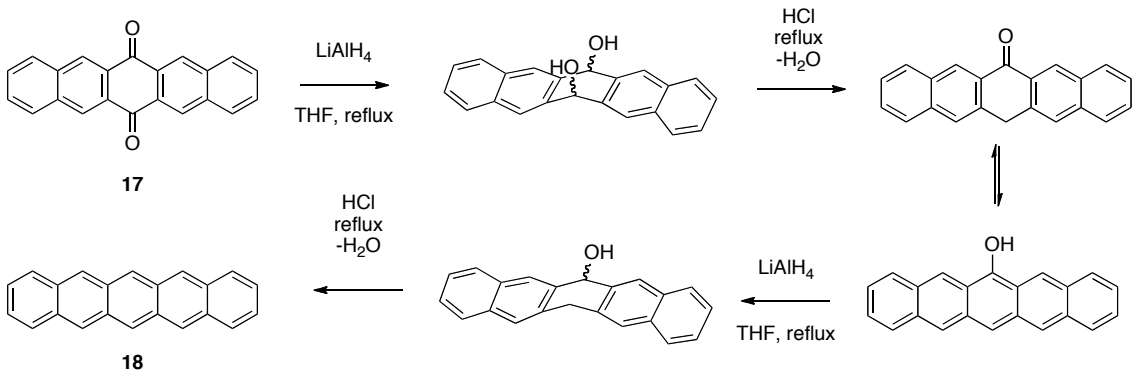

Scheme 60

Regarding the acene branch extension, several iterative approaches like Bergman cycloaromatization[224] or via zirconocene mediated cyclotrimerization[225] reactions have been developed in the context of pentacenes synthesis. Another method for the synthesis of acenes is a 4-fold aldol condensation between 2,5-dimethoxyhydrofuran and 1,2-benzene dialdehyde,[226,227] whereas a [4+2] cycloaddition reaction between *ortho*-quinodimethanes, prepared *in situ* applying Cava's reaction[228] starting from $\alpha,\alpha,\alpha',\alpha'$-tetrabromo *ortho*-xylenes, with 1,4-quinones, has been also employed to afford aromatic ring extended quinone derivatives.[229]

Having into account all these precedents for the synthesis of triphenylenes and extended acenes, and the electronic and structural properties requested for future molecular electronic applications, we designed several synthetic strategies for the preparation of differently π-extended Y-branched molecules.

224 (a) Bowles, D. M.; Anthony, J. E. *Org. Lett.* **2000**, *2*, 85-87. (b) Chow, S.-Y.; Palmer, G. J.; Bowles, D. M.; Anthony, J. E. Org. Lett. **2000**, *2*, 961-963.

225 (a) Takahashi, T.; Kitamura, M.; Shen, B.; Nakajima, K. *J. Am. Chem. Soc*. **2000**, *122*, 12876-12877. (b) Takahashi, T.; Li, S.; Huang, W.; Kong, F.; Nakajima, K.; Shen, B.; Ohe, T.; Kanno, K. *J. Org. Chem*. **2006**, *71*, 7967-7977.

226 Mallouli, A.; Lepage, Y. *Synthesis* **1980**, *6*, 689.

227 Miao, Q.; Lefenfeld, M.; Nguyen, T. Q.; Siegrist, T.; Kloc, C.; Nuckolls, C. *Adv. Mater*. **2005**, *17*, 497-412.

228 Cava, M. P.; Napier, D. R. *J. Am. Chem. Soc*. **1957**, *79*, 1701-1705.

229 (a) Miller, G. P.; Mack, J.; Briggs, J. *Proc. Electrochem. Soc.* **2001**, *11*, 202-206. (b) Swartz, C. R.; Parkin, S. R.; Bullock, J. E.; Anthony J. E.; Mayer A. C.; Malliaras, G. G.

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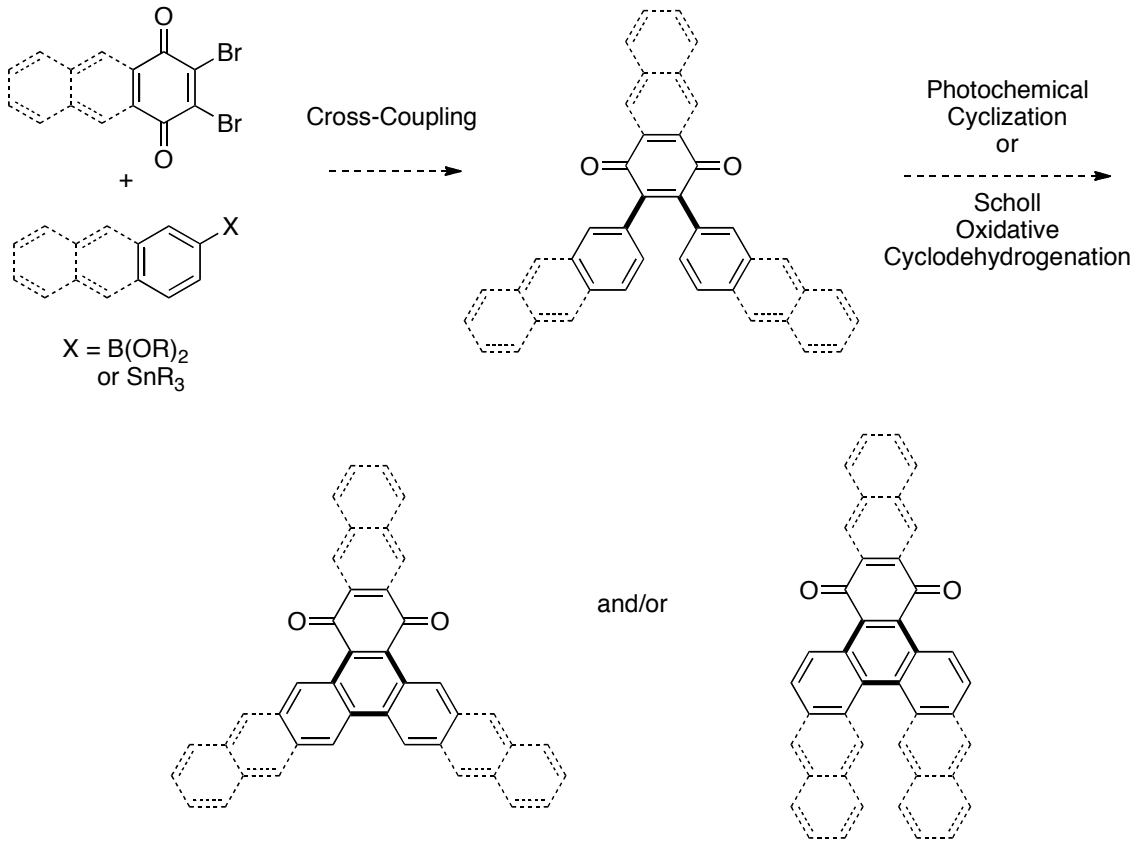
3.3 Synthesis of Y-Shaped Molecules: First Strategy[230]

Our first strategy is based on the cyclization of *ortho*-terphenyl derivatives following *strategy b* from *Scheme 58*. In our approach for the synthesis of large Y-shaped molecules, we planned to apply a double cross-coupling reaction between *ortho*-dibromoquinones (that can be later reduced or functionalized) and organoboronate or organostannane aryl compounds, which will be followed by a key photochemical or Scholl oxidative cyclodehydrogenation step (*Scheme 61*). As there are two possible positions where cyclization may occur, depending on the regioselectivity of the reaction starphene or helicene derivatives could be obtained. Moreover, depending on the acene extension of the starting material, after reduction of the quinone moieties, we could access to three equally branched or to C_2-symmetric Y-shaped polyarenes.



Scheme 61

230 Part of the work on the synthesis of Y-shaped molecules: first strategy was carried out in

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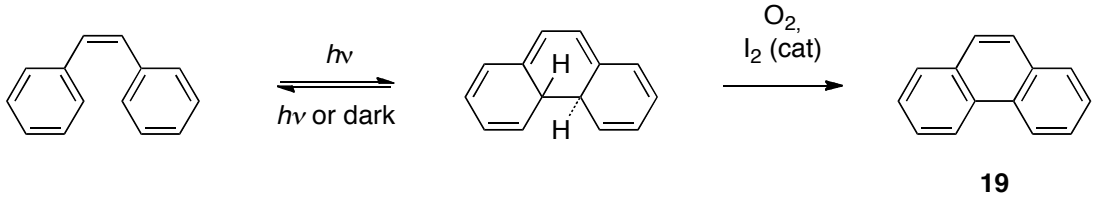
3.3.1 Precedents for the First Strategy

Photochemical reactions have been effectively applied for the synthesis of phenanthrenes starting with *cis*- or *trans*-stilbenes. The mechanism proceeds through reversible formation of dihydrophenanthrene intermediates that undergo hydrogen abstraction by an oxidant to give the corresponding phenanthrenes (**19**).[231]



Scheme 62

In their extensive work on photochemical cyclizations, Mallory and Mallory[232] studied the regiochemistry of the reaction, and its dependence on both, the electronic and the steric factors,[233] with a series of polyarenes where photocyclization may occur at different carbon atoms. According to their mechanism proposal through reversible dihydroaromatic intermediates, in sterically unhindered systems, the major product will be obtained from the intermediate with the greater aromatic resonance stabilization. As pointed out in the general introduction of PAHs, a way to assess stability to aromatic compounds is according to Clar's rule based on the localization of aromatic sextets.[234]

Experimentally, the photocyclization of dinaphthalene **20** gives a 62% yield of benzo[*g,h,i*]perylene (**21**) and dibenzo[*c,g*]phenanthrene (**22**), which derive from the electronically favored intermediate containing major stabilization with two benzene rings (see *Scheme 63*), and a 38% yield of dibenzo[*b,g*]phenanthrene (**23**) coming from electronically disfavored intermediate. Pentaphene **24**, which should derive from the electronically doubly unfavored dihydrointermediate,[232] is not observed in the photocyclization reaction.

231 Mallory, F. B.; Word, C. S.; Gordon, J. T. *J. Am. Chem. Soc*. **1964**, *86*, 3094-3102.

232 Mallory, F. B.; Mallory, C. W. *Organic Reactions*; Wiley & Sons: New York, **1984**; Vol 30, pp. 1-456

233 Laarhoven, W. H.; Cuppen, T. J. H. M.; Nivard, R. J. F. *Tetrahedron* **1970**, *26*, 4865-4881.

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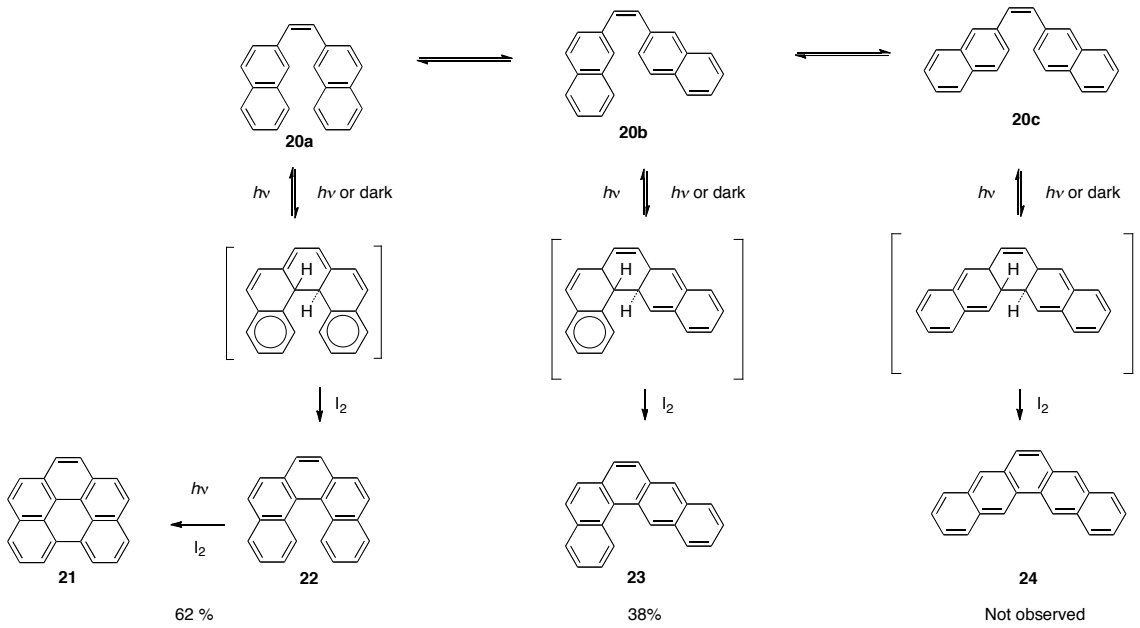

Scheme 63

An alternative to carry out cyclizations of *ortho*-terphenyls is the oxidative coupling in the presence of a Lewis acids (such as $AlCl_3$ and $FeCl_3$[235]), namely the Scholl reaction.[236,237] Among the wide examples on both intra- and intermolecular version of the oxidative aryl-aryl coupling for the synthesis of large polyaromatic system,[238] using different Lewis acids and conditions, a representative example illustrates the use of this reaction for the sythesis **26a-b** and **28** using $FeCl_3$ (*Scheme 64*).[239]

235 See: Sarhan, A. A. O.; Bolm, C. *Chem. Soc. Rev*. **2009**, *38*, 2730-2744 and references therein.

236 (a) Scholl, R.; Seer, C.; Weitzenböck, R. *Chem. Ber*. **1910**, *43*, 2202-2209. (b) Scholl, R.; Seer, C. *Liebigs Ann. Chem*. **1912**, *394*, 111-123**.** (c) Scholl, R.; Neumann, H. *Chem. Ber*. **1922**, *55*, 118-126. (d) Scholl, R.; Seer, C. *Chem. Ber*. **1922**, *55*, 330-341.

237 See earlier reviews: (a) Balaban, A. T.; Nenitzescu, C. D. In *Friedel-Crafts and Related Reactions;* Olah, G. A., Ed.; Interscience: New York, **1964**; Vol. 2, Part 2, p 979. (b) Kovacic, P.; Jones, M. B. *Chem. Rev.* **1987,** *87,* 357-379.

238 See recent reviews: (a) Sergeyev, S.; Pisula, W.; Geerts Y. H. *Chem. Soc. Rev*. **2007**, *36*, 1902-1929. (b) Wu, J.; Pisula, W.; Müllen, K. *Chem. Rev*. **2007**, *107*, 718-747.

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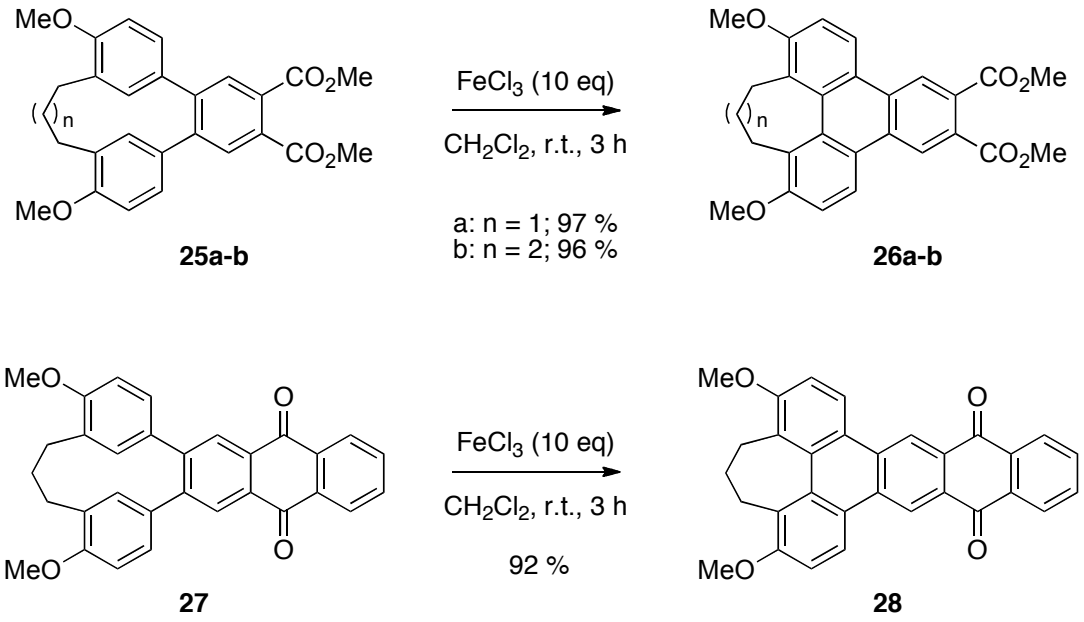

Scheme 64

It has been experimentally observed that Scholl reaction usually proceeds with low selectivity. According to theoretical and experimental work, oxidative cyclization works better in large polyphenylenes, as a consequence of the high insolubility of larger systems that precipitate after the product formation, rather than with smaller triphenylenes, which tend to oligomerize during the course of the reaction.[240] Directing groups in electrophilic aromatic substitution predict the outcome of the Scholl reaction in substituted arenes, with activating groups (like OMe), directing *ortho* and *para* bond formation, while deactivating *meta*-directing groups (like NO_2) inhibit the reaction.

3.3.2 Development of the First Strategy

Initially, we chose synthetic model systems applying the cross-coupling reaction between organometallic naphtyl derivatives and 2,3-dibromo-1,4-naphtho- or anthraquinone to synthetically explore their differences and similarities with phenylenes regarding their chemical reactivity and the electronic influence of the quinone in the regioselectivity on the photochemical reaction according to the precedents.

240 (a) Rempala, P.; Kroulik, J.; King, B. T. *J. Am. Chem. Soc.* **2004**, *126*, 15002-15003. (b)

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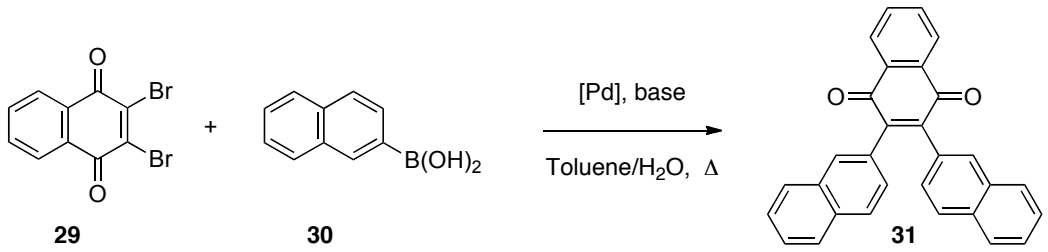
Starting with 2.2 equiv of commercially available 2-naphthalene boronic acid (**30**) and 2,3-dibromo-1,4-naphthoquinone (**29**), under thermal conditions, the double Suzuki cross-coupling reaction was performed in the presence of base (Na_2CO_3) and palladium catalyst [$PdCl_2$dppf] to give 2,3-dinaphthyl-1,4-naphthoquinone (**31**) in 68% yield. When the reaction was performed under similar conditions ([$Pd(PPh_3)_4$], K_2CO_3) but promoted with microwave irradiation, reaction time was considerably reduced and the yield was increased up to 95% (*Scheme 65*). Generally, we found that in related systems, microwave conditions enhanced the reactivity and selectivity of the reaction, whereas, as shown for similar reactions,[241] the presence of an excess of water is crucial to obtain good selectivities and yields.



29 **30** **31**

Conditions
Termal: **(A)** $PdCl_2$dppf (5 mol%), Na_2CO_3 (5 equiv), H_2O/toluene, 100 ºC, 5h, **68%**
Microwave: **(B)** $Pd(PPh_3)_4$ (5 mol%), K_2CO_3 (6 equiv), H_2O (50 equiv.), Toluene, 120 ºC (MW), 1.5 h, **95%**

Scheme 65

To prepare homologous 2,3-napthyl-1,4-anthraquinone (**34**), firstly dibromination of commercially available 1,4-anthraquinone (**32**) was performed to give **33** in 80% yield. Double cross-coupling reaction of **33** with 2.4 equiv of 2-naphthalene boronic acid (**30**) (*Scheme 66*), under similar microwave conditions as for **31**, afforded the desired **34** in 81% yield.

241 Shimizu, M.; Nagao, I.; Tomioka, Y.; Hiyama T. *Angew. Chem. Int. Ed*. **2008**, *47*, 8096-

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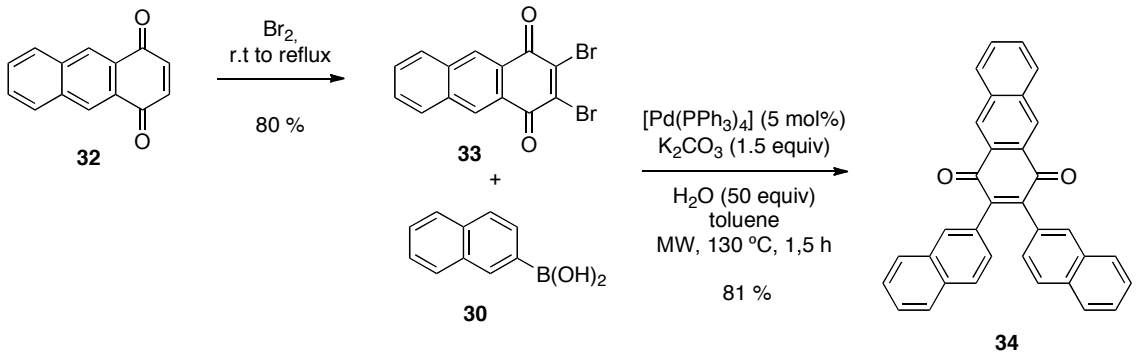
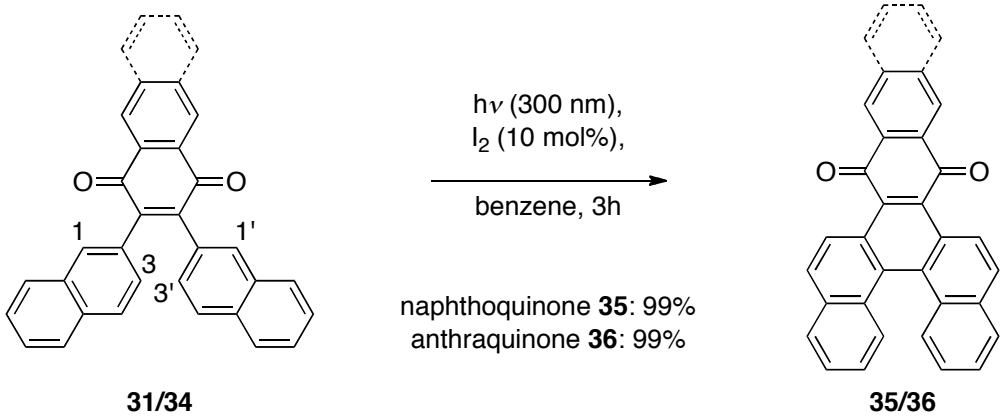


Scheme 66

Both 2,3-naphtylquinones precursors, **31** and **34**, were submitted to photocyclization by irradiating with 300 nm lamps according to the standard procedure (*Scheme 67*);[232] using substoichiometric amounts of iodine to promote oxidation, in the presence of air (O_2) in benzene. In both cases, cyclization occurred exclusively at the C1-C1' position of the naphtyl branches and quantitative yield of dinaphtho[2,1-*a*:1',2'-*c*]anthra- or tetracene-11,18-dione helical products **35** and **36** were isolated (*Scheme 67*). These compounds are the ones expected from the electronically most favored intermediate and thus, no electronic influence from the quinone moiety is observed.



Scheme 67

Moreover, to promote a second cyclization in compounds **31**/**34** and force the formation of perylene derivatives, which also have potential applications as molecular wires and in organic photovoltaic devices,[242] both **35** and **36** products

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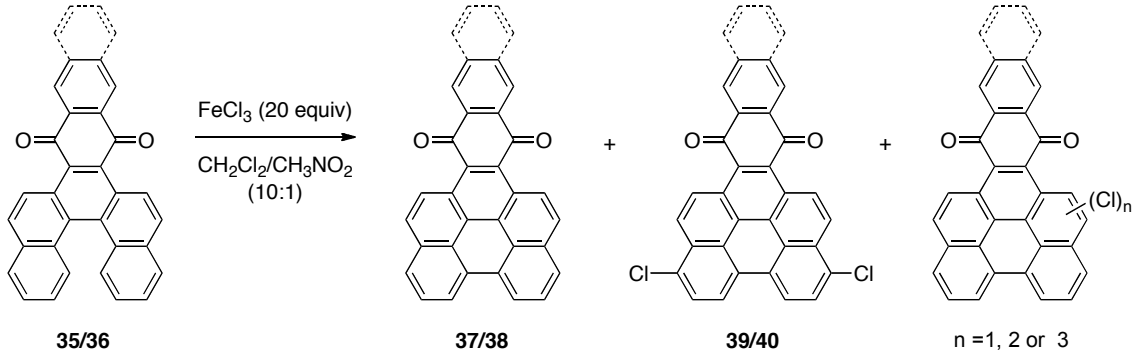
were submitted to the oxidative Scholl reaction using $FeCl_3$ as the promoter. Oxidative cyclodehydrogentation took place and perylene derivatives **37**/**38** were formed under the reaction conditions. As it has been previously reported for oxidative couplings on polyarene systems when $FeCl_3$ is used, reaction gave a mixture of the desired product along with polychlorinated products (*Scheme 68*).[240,243] Compounds **37**/**38** could be identified by proton NMR although pure products could not be isolated. The mixtures of mono-, di-, and trichlorinated derivatives were detected by mass spectroscopy, wherein 1,6-dichlorinated products **39**/**40** structures could be confirmed by 2D NMR experiments.



Scheme 68

Despite the recent new methodologies developed for the synthesis of helicenes[244] as a result of their increasing interest for material application, these results show the straightforward procedure and effectiveness of microwave cross-coupling reaction followed by photochemical reaction for the synthesis of helicene **35** and its homologue **36**. Moreover, combination of photochemical cyclization and subsequent oxidative Scholl reaction can be combined for the preparation of perylenes products (**37**/**38**) through a stepwise double oxidative cyclization process. Nonetheless, some common limitations like polymerization or halogenation side reactions for the Scholl cyclization must be taken into account. All four products could be reduced or functionalized through their quinone moieties.

243 Zhou, Y.; Liu, W.-J.; Zhang, W.; Cao, X.-Y.; Zhou, Q.-F.; Ma, Y.; Pei, J. *J. Org. Chem.* **2006**, *71*, 6822–6828.

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To obtain starphene derivatives starting with 2,3-dinaphthyl-1,4-naphthoquinone (**31**), we needed to change the regioselectivity of the intramolecular oxidative coupling. Therefore, different conditions were explored to connect the C3-C3'-positions in the cyclization (see *Scheme 67*). Initially, photochemical reaction conditions were explored by changing the frequency of irradiation lamps (254 or 350 nm) or by using an improved photocyclization procedure developed by Katz *et al*.[245] This consists in the addition of equimolar amounts of iodine as oxidant and propylene oxide to quench the HI formed. Nonetheless, in none of the conditions tried, neither trinaphthylene-5,18-dione (**41**), naphtho[1,2-*h*]pentaphene-11,16-dione (**43**), or its anthracenic analogues, **42** and **44**, that would derived from electronically unfavored intermediates were observed. Perylene derivatives **37**/**38**, which could be formed by a second cyclization of the helical product were neither detected (*Figure 42*).

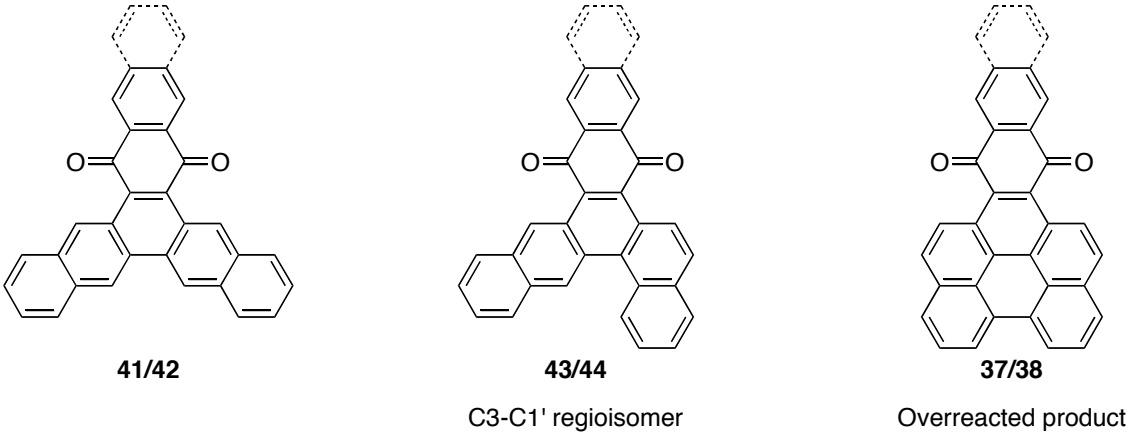

*Figure 42: Regioisomers and overreacted product not observed on the photocyclization of **31** and **34***

Furthermore, we applied the Scholl reaction to substrates **31**/**34**. Using $FeCl_3$, no cyclized product was observed and only a dichlorinated product **45** at C1 position of the naphtyl moieties was detected. Having now the positions C1-C1' of the naphthyl substituents chlorinated, we tried the photochemical reaction or to force the conditions of the Scholl reactions by increasing the temperature, to obtain the

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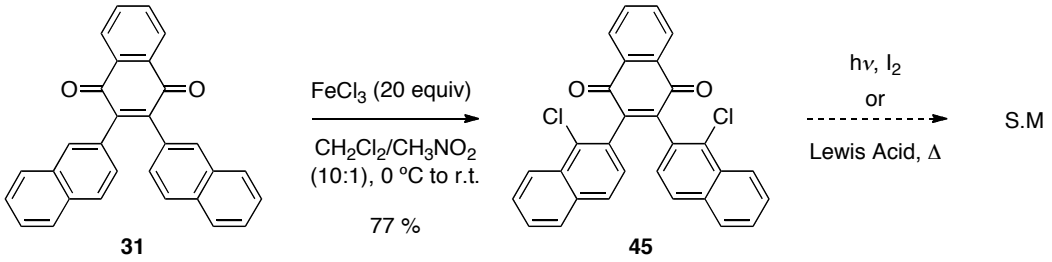
cyclized starphenes. However, only starting material was recovered showing that the C3 positions in these systems (*Scheme 69*).



Scheme 69

2.2.2.1 Sterically Hindered Anthracene Branches

We decided to explore the cross-coupling reaction with new anthracenyl boronate derivatives. Thus, anthracene branches bearing hindering substituents at the central ring (*Figure 43*), could force oxidative cylcization to take place at the C3 positions instead of C1 position of the anthracene branches.

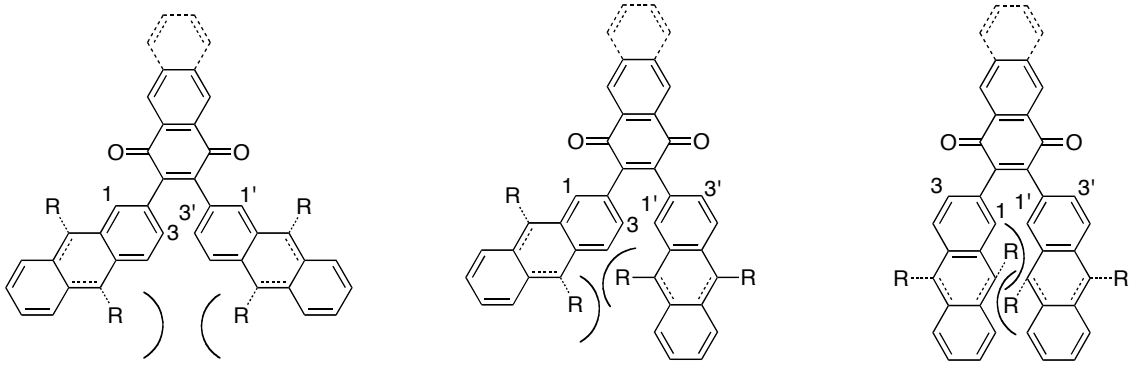
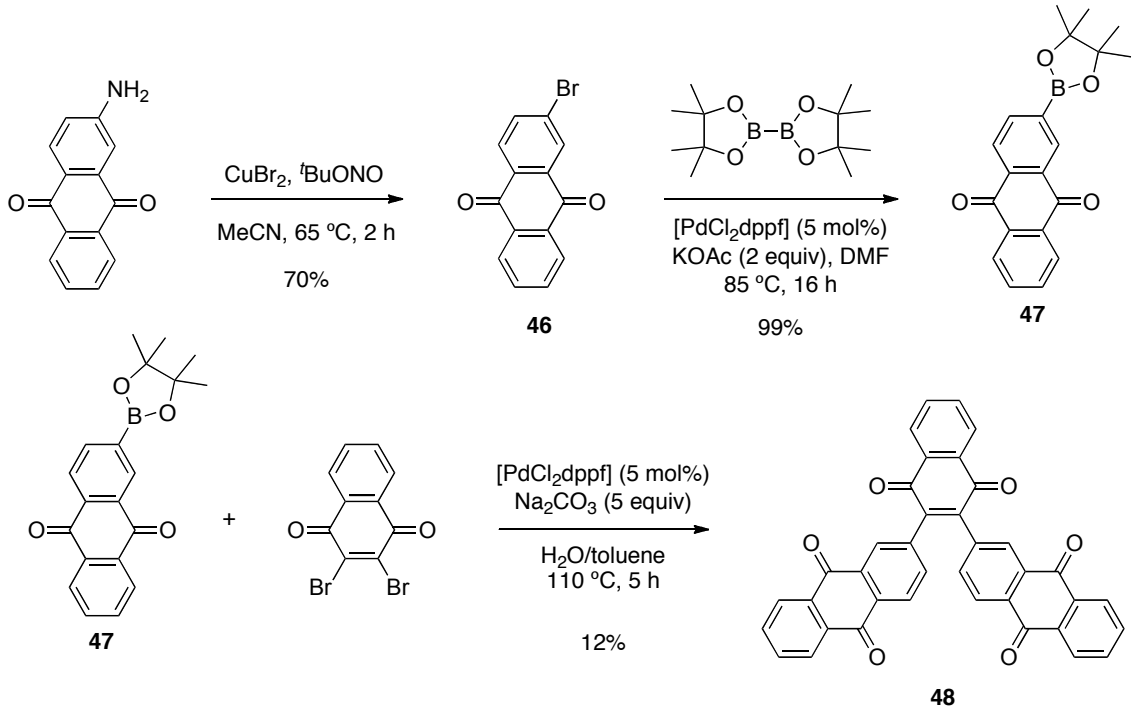


Figure 43: Sterically hindered models after oxidative cyclization.

Dianthraquinone derivative **48** was prepared in three steps starting with commercially available 2-aminoanthraquinone (*Scheme 70*). Following the described procedure, Sandmeyer reaction yielded in 30% of 2-bromo-9,10-anthraquinone **46**.[246] This could be improved by using a related procedure, which yielded the product in 70%, although it was contaminated with 6% of unsubstituted

anthraquinone.[247] Anthraquinone **46** was transformed into the organometallic boron pinacolate derivative **47** under standard palladium-catalyzed conditions using [$PdCl_2$dppf] and KOAc. Compound **47** was highly sensitive to acid or basic media and could not be purified by silica or alumina column chromatography, and therefore, was used without further purification in the next step. A Suzuki reaction with 2,3-dibromo-1,4-naphthoquinone **29** was performed, using [$PdCl_2$ddpf] and Na_2CO_3, which yielded the desired compound **48** in only 12% (*Scheme 70*). Attempts were made to synthesize **48** via a Stille coupling reaction, but again, the tributylstannane analogue of **47** could not be purified which led to low yields in the cross-coupling reaction.



Scheme 70

Derivative **48** did not react under photochemical irradiation with 254 or 300 nm lamps[231] and only starting material could be reisolated. Complete conversion was achieved using Katz[245] procedure at higher frequency with 350 nm lamps, although, in this case, a complex mixture of products was obtained. Alternatively, when oxidative cyclodehydrogenation reaction was carried out in the presence of DDQ as

247 Lee, S. K.; Yang, W. J.; Choi, J. J.; Kim, C. H.; Jeon, S.-J.; Cho, B. R. *Org. Lett.* **2005**, *7,*

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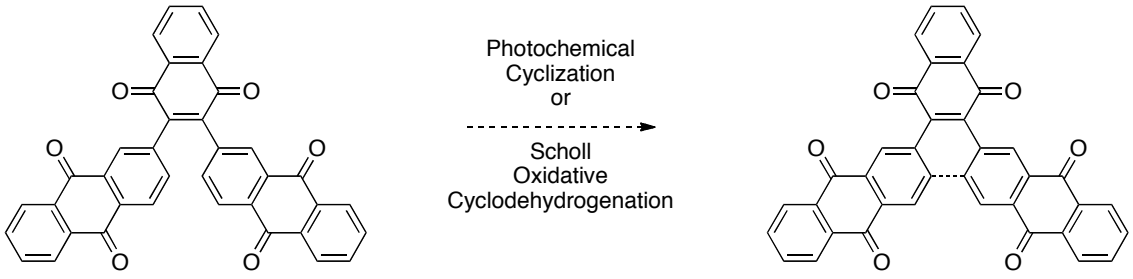
oxidant and methanesulfonic acid,[248] not complete conversion was achieved and an unidentified product that did not correspond to the desired **49** was observed in the crude mixture.



Scheme 71

To avoid the possible negative influence of electron-withdrawing anthraquinone moieties, we decided to prepare 2-bromo-9,10-dimethylanthracene (**50**) according to the described methylation/dehydroxaylation procedure sequence (*Scheme 72*).[249] Compound **50**, bearing two methyl groups to favor the final cyclization at the less sterically hindered C3-C3' position of the anthracenic branches, is a promising precursor for the preparation of the corresponding starphene derivative. Reaction of **50** with bis(pinacolato)diboron under palladium-catalyzed conditions gave the boronpinacolate dimethylanthracene derivative **51** in 36% yield. The presence of many byproducts in the crude mixture, including debrominated 2,9-dimethylanthracene (**52**), and the remaining bis(pinacolato)diboron starting material, made the isolation of pure compound **51** difficult (*Scheme 72*).

248 Zhai, L.; Shukla, R.; Rathore, R. *Org. Lett.* **2009**, 11, 3474-3477.

249 Keana, J. F. W.; Prabhu, V. S.; Ohmiya, S.; Klopfenstein, C. E. *J. Org. Chem.* **1986**, *51*,

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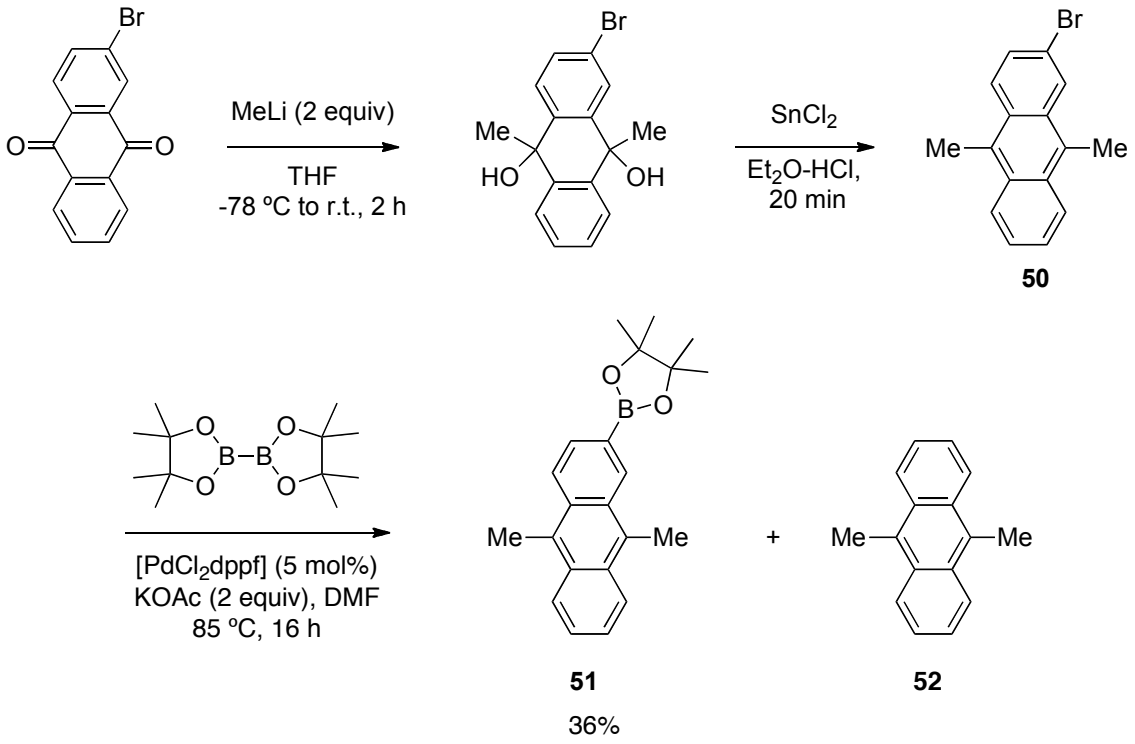
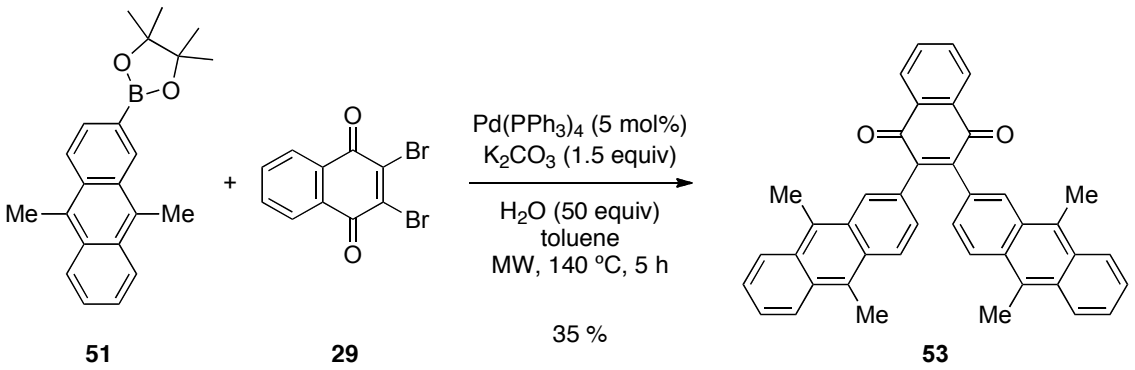


Scheme 72

Suzuki cross-coupling reaction, with $[Pd(PPh_3)_4]$ and K_2CO_3 in toluene, of **51** with 2,3-dibromo-1,4-naphtoquinone (**29**) under microwave irradiation gave the desired product **53** in low yield (35%) (*Scheme 72*). Due to the low yield and instability of compound **53** which decomposed in solution, no cyclization was performed with this compound.



Scheme 73

We also attempted the synthesis of compound **54**. The proposed synthesis for the designed molecule consists, again, in the cross-coupling reaction of 2,3-

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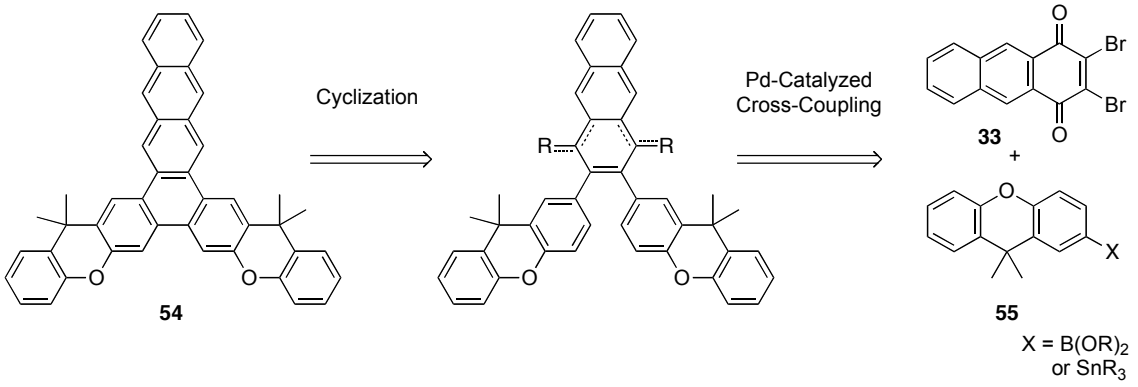
dibromoanthraquinone **33** and organometallic xanthene derivative **55**, followed by photocyclization or oxidative Scholl reaction (*Scheme 74*).



Scheme 74

Starting from commercially available xanthone, the dimethylation with Me_3Al[250] afforded the desired xanthene **56** in almost quantitative yield. Bromination of xanthene using 1.1 equiv of Br_2 gave the 2,7-dibrominated derivative **58** as the major product. When 0.6 or 0.5 equiv of bromine were added, a mixture of mono- and dibrominated adducts, **57** and **58** respectively, together with unreacted starting material were obtained. The separation of mono- and dibrominated products by column chromatography could not be achieved, while starting material could be separated and recovered (*Scheme 75*).

250 Nowick, J. S.; Ballester, P.; Ebmeyer, F.; Rebeck, J. *J. Am .Chem. Soc*. **1990**, *112*, 8902-

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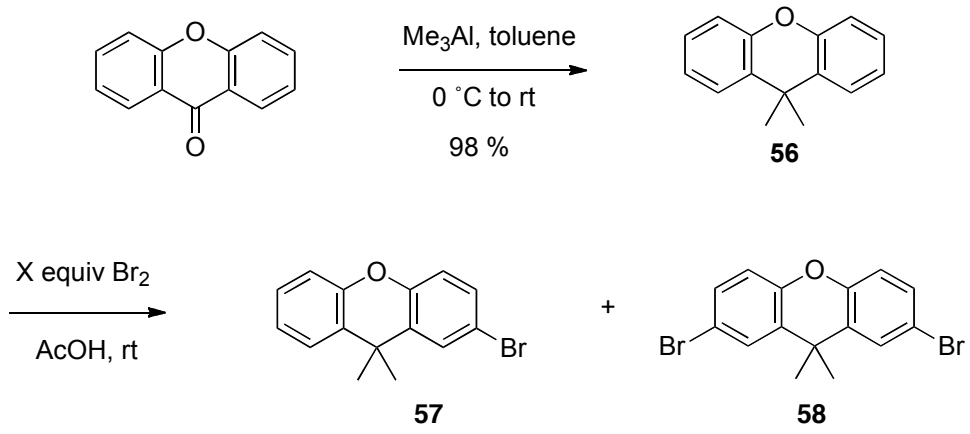
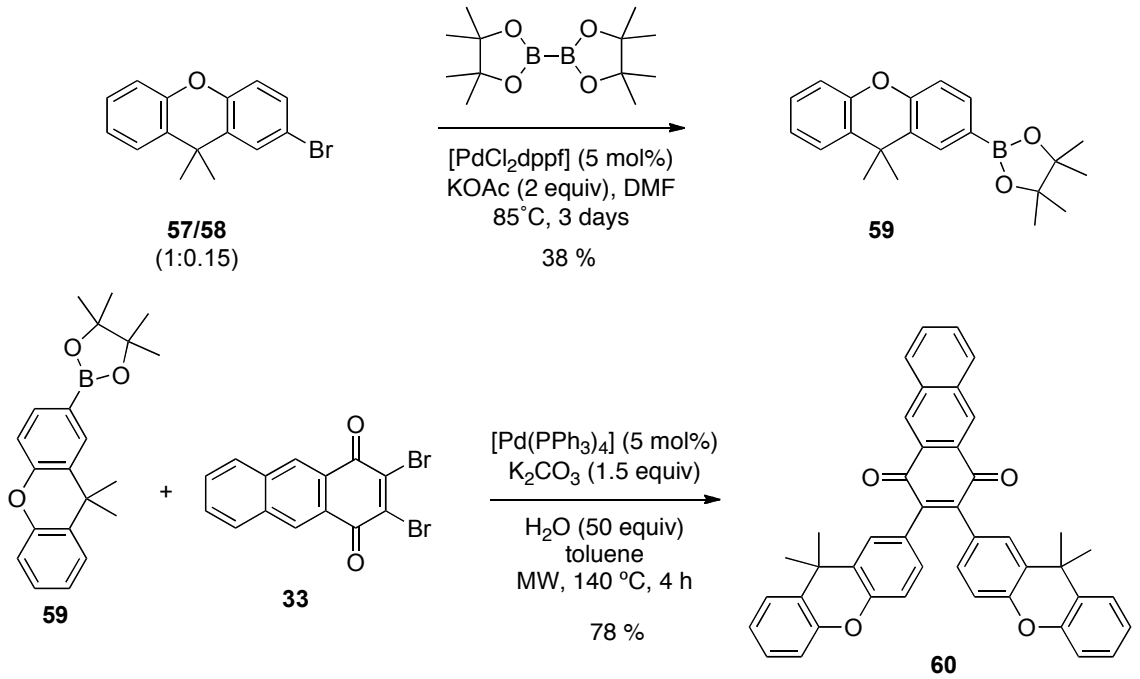


Scheme 75

Using the same conditions as before, palladium-catalyzed reaction with bis(pinacolato)diboron reagent, gave the corresponding organometallic derivative **59** in moderate yield (38%). As in related substrates, long reaction times were required and many byproducts were detected in the crude mixture. For the Suzuki cross-coupling with 2,3-dibromo-1,4-anthraquinone (**33**), using $[Pd(PPh_3)_4]$ as the catalyst and K_2CO_3, under microwave irradiation, 78% yield of pure product **60** was isolated (*Scheme 76*).



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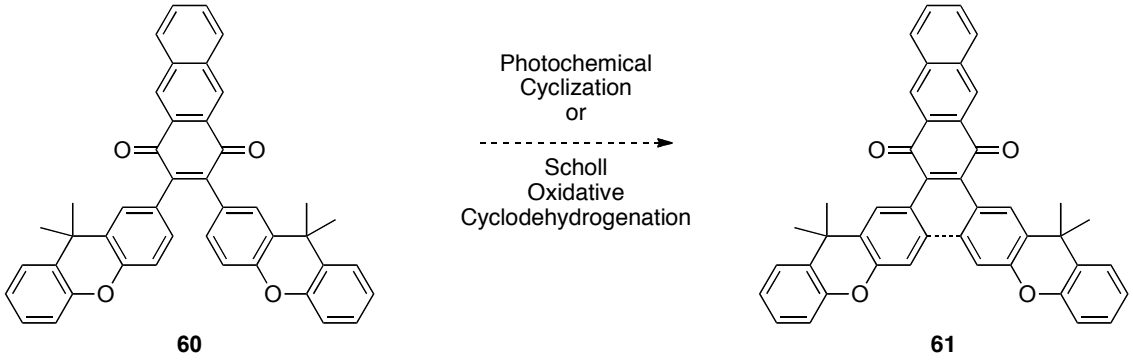
2,3-Bis(9,9-dimethyl-9*H*-xanthen-2-yl)anthracene-1,4-dione (**60**) was submitted to photocyclyzation reaction using different irradiation frequencies. When **60** was irradiated with 254 nm lamps,[232] no reaction was observed after 24 h. When irradiation frequencies were increased to 300 or 350 nm, under long reaction times, conversion of starting material could be observed, but a complex mixture of products was obtained. Oxidative cyclodehydrogenation reaction according to the standard procedure $FeCl_3$[235] or by using DDQ as oxidant and methanesulfonic acid[248] was also tested at different reaction temperaturesHowever, starting material or complex mixtures were observed in all cases.



Scheme 77

Due to the incompatibilities of 2,3-bis(9,9-dimethyl-9*H*-xanthen-2-yl)anthracene-1,4-dione (**60**) under the photochemical or oxidative conditions, we explored a second approach for the synthesis of the designed molecule **54**. Thus, cyclization reaction (photochemical or oxidative cyclodehydrogenation) of **65** would be performed in the first steps of the synthesis (*Scheme 78*). Extension of the xanthene branches would be accomplished by the condensation of hydroxybenzoic acid and dihydroxy derivative **63** as reported for the synthesis of xanthones.[251,252] Finally, dialkylation of quinone moieties with Me_3Al would deliver compound **54** (*Scheme 78*).

251 Pillai, R. K. M.; Naiksatam, P.; Johnson, F.; Rajagopalan, R.; Watts, P. C.; Cricchio, R.; Borras, S. *J. Org. Chem*. **1986**, *51*, 717–723.

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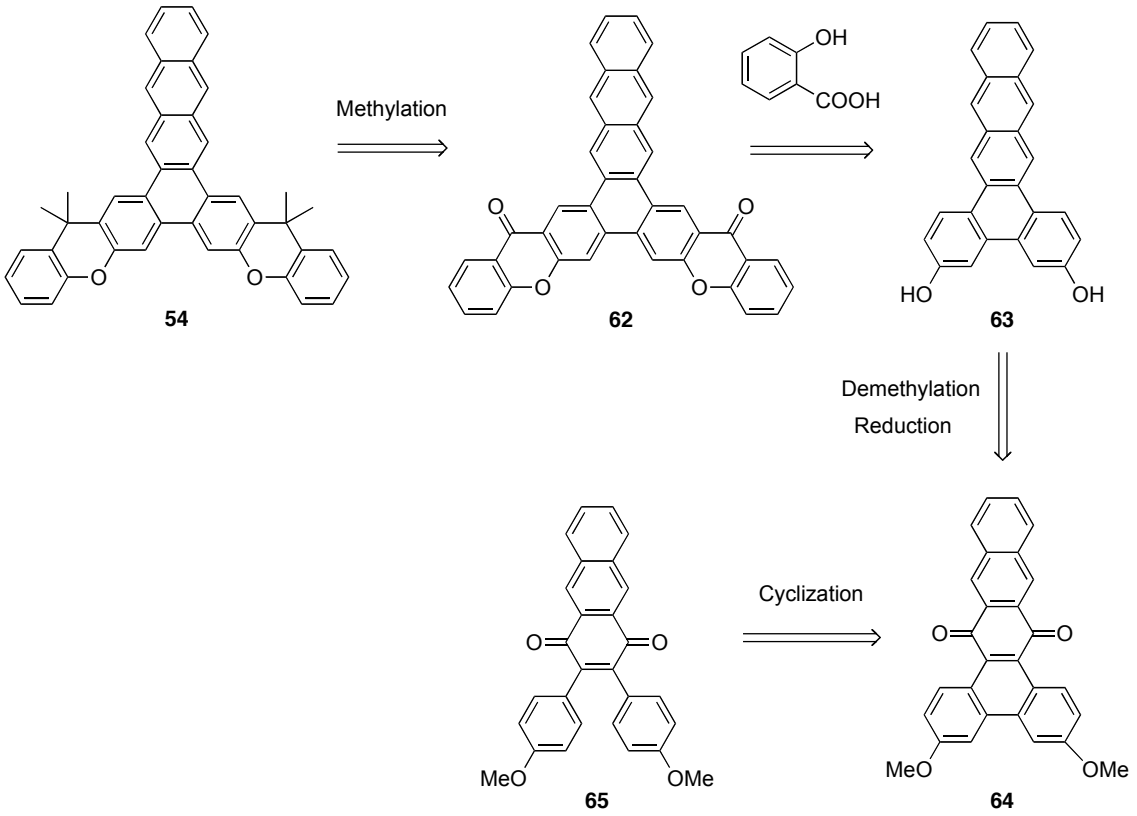
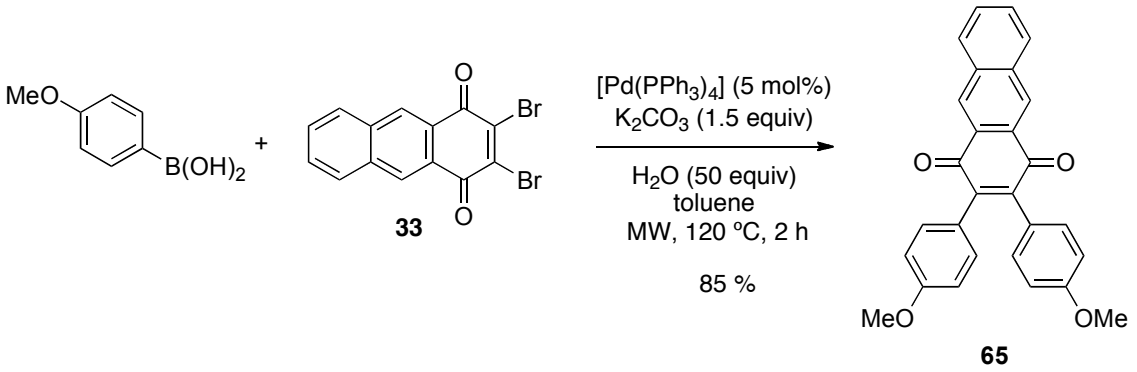


Scheme 78

Suzuki cross-coupling reaction between 4-methoxyphenylboronic acid and the 2,3-dibromo-1,4-anthraquinone **33** under microwave irradiation, using $[Pd(PPh_3)_4]$, K_2CO_3, toluene and 50 equiv of H_2O, could be performed in 2 hours with 85% yield to yield **65** (*Scheme 79*).



Scheme 79

When quinone **65** was submitted to photochemical reaction under different conditions and irradiation frequencies, starting material and/or complex mixture of

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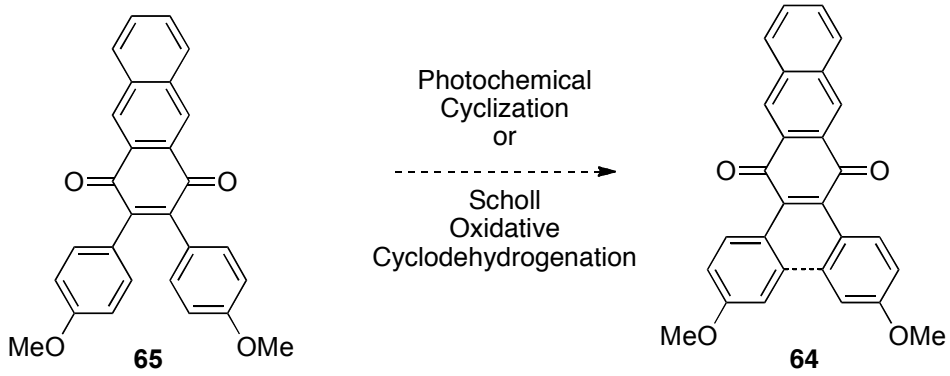
Scholl reaction. When $FeCl_3$, ceric ammonium nitrate (CAN), or copper triflate were used as the oxidant, only complex mixtures were obtained and the desired product could not be identified in the crude mixture. By using DDQ in the presence of methanesulfonic acid, an unknown product similar to starting material could be detected, but could not be characterized or isolated pure.



Scheme 80

To avoid a possible incompatibility of the quinone-system under the reaction conditions, we decided to reduce the quinone prior to cyclization. Clemmensen reduction of **67** with Zn led to unchanged starting material. When $LiAlH_4$ hydride was used as the reducing agent followed by treatment with HCl, the conversion was not complete and a 37% of acene **67** was obtained together with 18% of penol **68** (*Scheme 81*). The observed shift of the OH groups, probably takes place through an elimination-addition process. As reported,[223] reduction takes place through a four-step sequence via alcohol intermediates. Therefore, we repeated twice the reduction/dehydration sequence and a 45% of desired 2,3-bis(4-methoxyphenyl)antracene (**67**) could be isolated.

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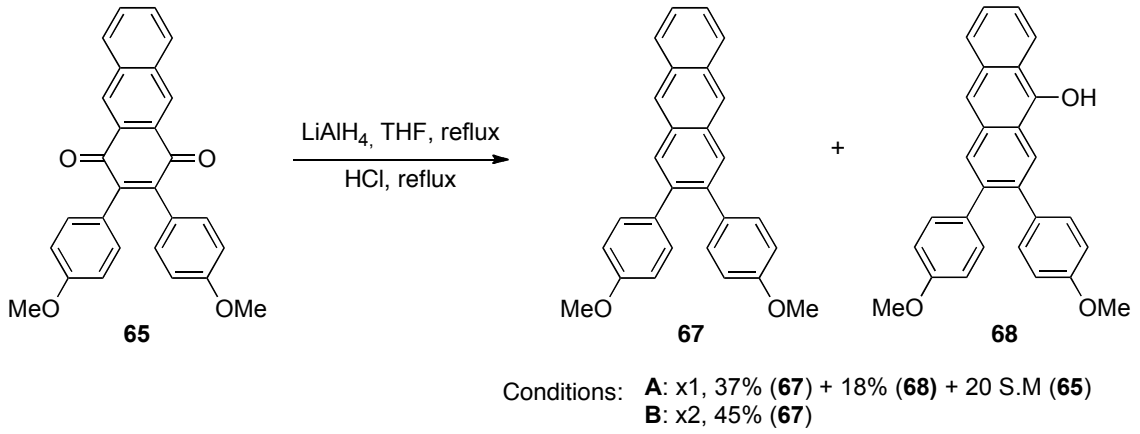
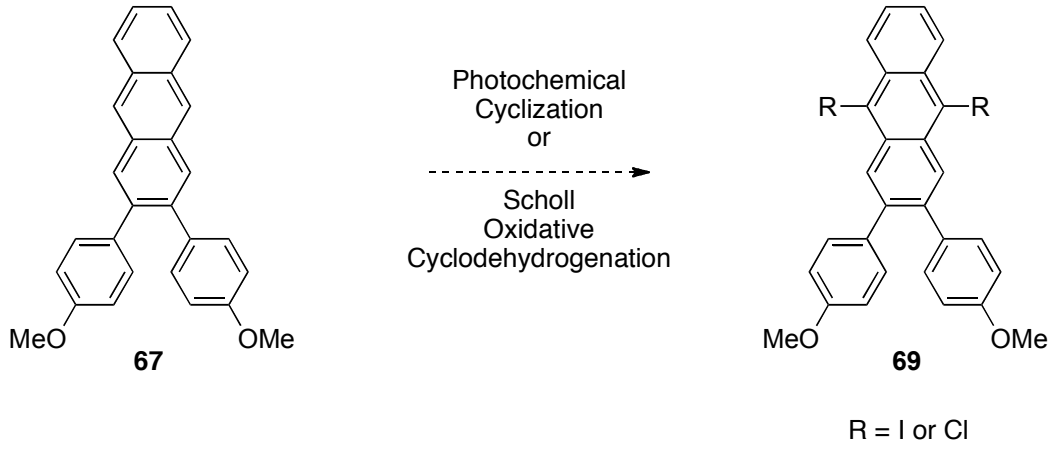


Scheme 81

Compound **67** was then submitted to cyclization under photochemical or oxidative conditions. However, the central ring of the anthracene was too reactive and only oxidation (leading to quinone under photochemical conditions or chlorination when $FeCl_3$ was used) at the positions 9 and 10 of the anthracene (see **69**) was assumed to be formed according to NMR and mass spectrometry (*Scheme 82*).



Scheme 82

All these results show the present difficulties on the cyclization step reaction for the explored *ortho*-terphenyl systems. Thus, future work within this approach should focus on the preparation of the triphenylene core in an alternative manner. Recently Hiyama *et al.*[253] have reported a straightforward and high-yielding approach for the palladium-catalyzed annulation of 9,9-dimethyl-9-stannafluorenes (**70**) with aromatic 1,2-dihaloarenes to form phenanthrenes like **71** (*Scheme 83*).

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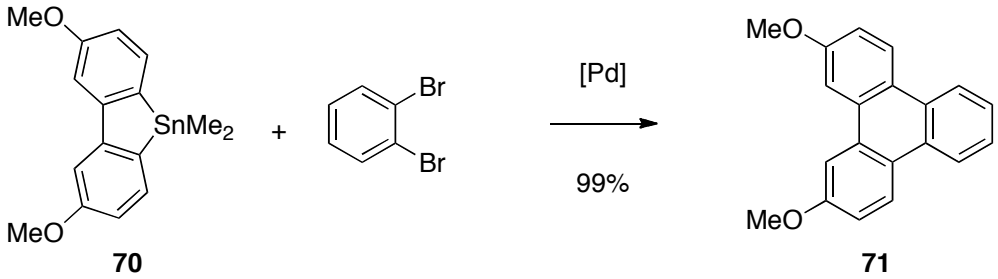


70 **71**

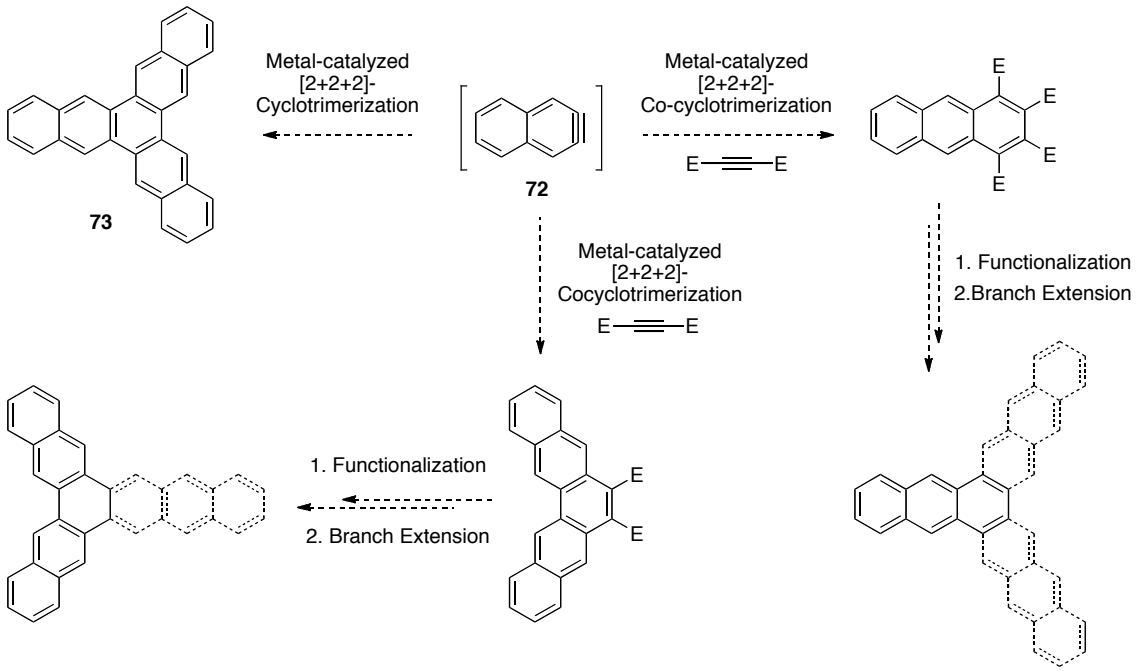
Scheme 83

Annulation reaction with 2,3-dibromo-1,4-anthraquinone could be performed to obtain desired compound **65** that could be followed by the already proposed way for the xanthene extended branches shown in *Scheme 78*.

In parallel to this first approach, a second strategy for the synthesis of starphenes was also developed in this work.

3.4 Synthesis of Y-Shaped Molecules: Second Strategy

Our second approach for the divergent synthesis of starphenes is based on the preparation of naphthalyne **72** as the main building block. Initially, as in *strategy a* from *Scheme 58*, the preparation of naphthalyne derivatives will allow us to apply a palladium-catalyzed [2+2+2]-cyclotrimerization reaction to form trinaphtylene (heptastarphene-(2.2.2), **73**). In addition, in the presence of activated alkynes, naphthalyne can undergo metal-catalyzed co-cyclotrimerization reactions. Depending on the palladium catalyst and the amount of alkyne, chemoselective reaction will lead to pentaphene or anthracene derivatives that can be further functionalized for the preparation of C_2 or C_3-symmetric starphenes (*Scheme 84*) like in *strategies d* and *e* shown in *Scheme 58*.



Scheme 84

3.4.1 Precedents for the Second Strategy

Arynes[254] are extremely reactive species that must be generated in situ. Common methods employed for the generation of *ortho*-arynes, are based either on the generation of aryl anions by treatment of a strong bases ortho to a leaving group[255] or by treatment of *ortho*-dihalogenbenzene in the presence of metals like Mg, Li[256] or *n*-BuLi[257] to promote metal-halogen exchange followed by α,β-elimination. Another methodology is based on the thermal or photochemical decomposition of zwitterionic species[258] or oxidation of 1-aminobenzotriazol derivatives via nitrene species that undergo decomposition leading to benzyne (**76**).[259] Although these methods are useful for the generation of benzynes, their tolerance to certain functional groups is limited. In 1983, Kobayashi described a mild and versatile

254 See review: Wenk, H. H.; Winkler, M.; Sander, E. *Angew. Chem. Int. Ed*. **2003**, *42*, 502-528, and references therein.

255 Caubère, P. *Chem. Rev*. **1993**, *93*, 2317-2334

256 Wittig, G. *Org. Synth*. **1959**, *39*, 75 (Coll. Vol. 4, 1963, 964).

257 Gilman, H.; Gorsich, R. D. *J. Am. Chem. Soc*. **1956**, *78*, 2217-2224.

258 Buxton, P. C.; Fensome, M.; Heaney, H.; Manson, K. G. *Tetrahedron* **1995**, *51*, 2959-2968.

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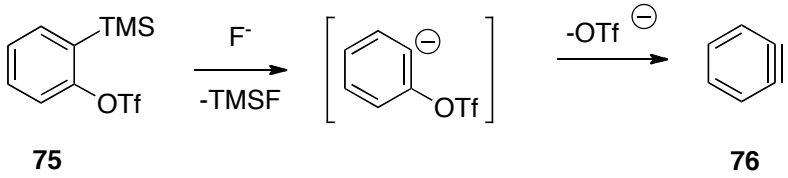
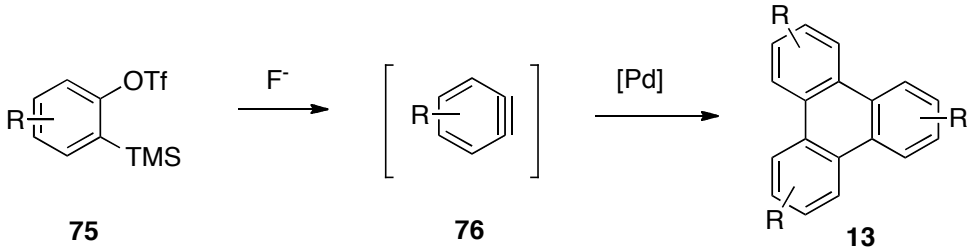
method for the in situ preparation of benzyne (**76**) through the fluoride-induced 1,2-elimination of *ortho*-silylaryltriflates **75** (*Scheme 85*).[260]



Scheme 85

In 1998, Guitián and co-workers reported the trimerization reaction of *ortho*-silylaryltriflates in the presence of palladium(0) catalysts for the synthesis of triphenylenes derivatives.[261] The best results were obtained in the presence of 10 mol% of $[Pd(PPh_3)_4]$, CsF or *n*-Bu_4NF as fluoride sources, in CH_3CN at room temperature.



Scheme 86

The mechanism proposed for the cyclotrimerization of arynes shown in *Scheme 87* is similar to the mechanism for [2+2+2]-cycloadditions of alkynes.[262]

260 Himeshima, Y.; Sonada, T.; Kobayashi, H. *Chem. Lett*. **1983**, 1211-1214.

261 Peña, D.; Escudero, S.; Pérez, D.; Guitián, E. *Angew. Chem. Int. Ed*. **1998**, *37*, 2659-2661. (b) Romero, C.; Peña, D.; Pérez, D.; Guitián, E. *Chem. Eur. J*. **2006**, *12*, 5677-5684.

262 Recent review: Gandon, V.; Aubert, C.; Malacria, M. *Chem. Commun*. **2006**, 2209-2217,

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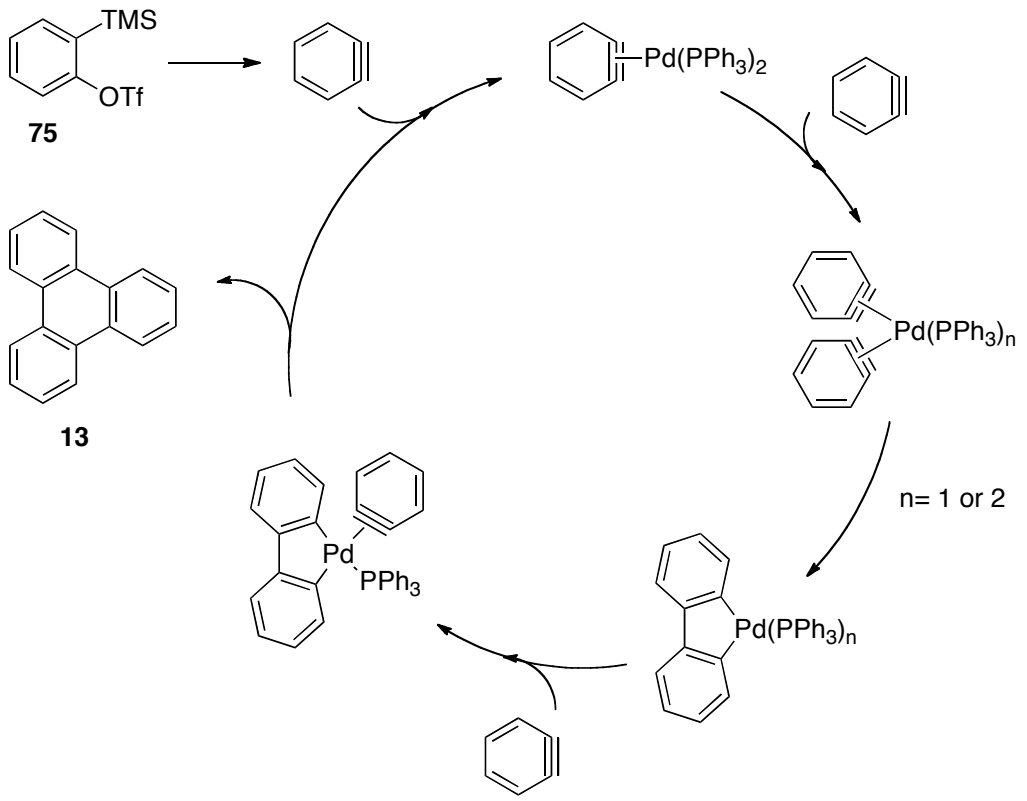

Scheme 87

The palladium-catalyzed [2+2+2]-cocycloaddition reaction of aryne with electron-deficient activated alkynes proceeds with remarkable chemoselectivity depending on the palladium catalyst and the amount of alkyne.[263,264] Thus, dimethylacetylenedicarboxylate (DMAD) undergo [2+2+2]-cocycloaddition with the in situ prepared arynes in the presence of palladium(0) to give either phenanthrene or anthracene derivatives depending on the reaction conditions (*Scheme 88).*

263 (a) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Am. Chem. Soc.* **1999**, *121*, 5827-5828. (b) Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *J. Org. Chem.* **2000**, *65*, 6944-6950.

264 For a recent review of palladium-catalyzed cycloaddition reactions of arynes, see: Guitián, E.; Pérez, D.; Peña, D. In *Topics in Organometallic Chemistry*; Tsuji, J., Ed.; Springer-

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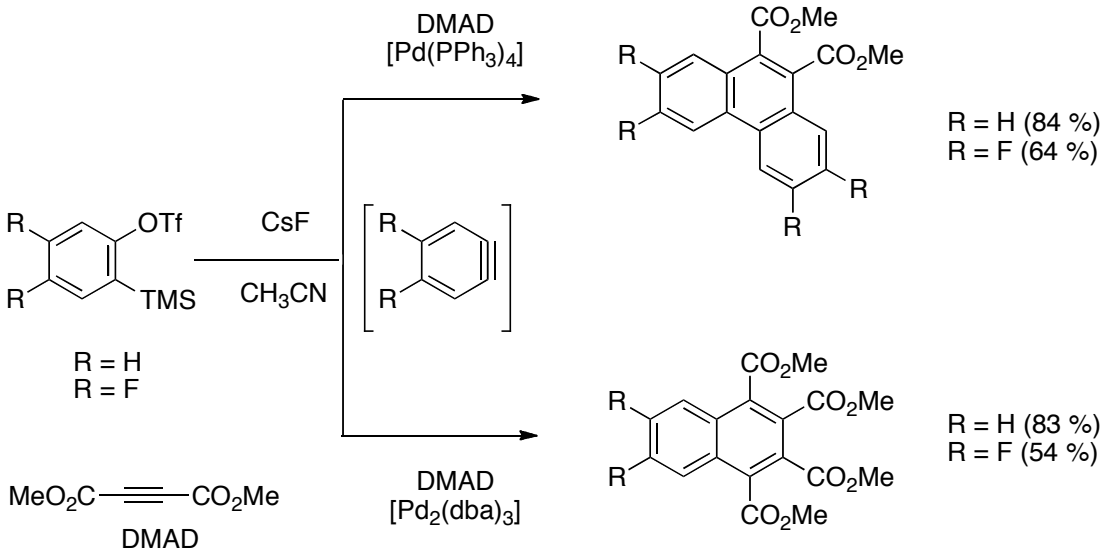
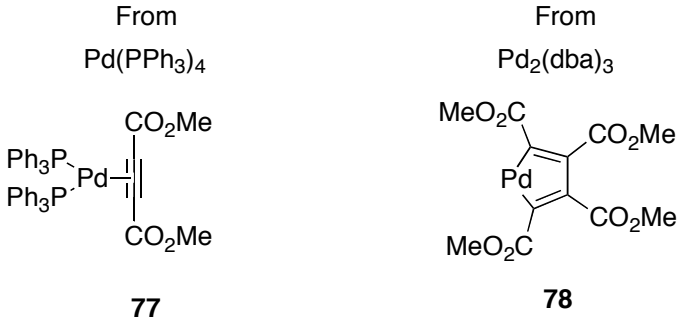


Scheme 88

The chemoselectivity in this reaction is explained by the possible formation of two different palladium complexes as intermediates, which will depend on the nature of the ligands. For instance, when the reaction is promoted by $[Pd(PPh_3)_4]$ it is assumed the formation of intermediate **77**, where the strongly coordinated triphenylphosphine ligands prevent the coordination of another alkyne, reacts with two arynes to afford the phenanthrenes products. On the other hand, in the case of $[Pd_2(dba)_3]$, presumably the catalyst reacts with two alkynes to give palladacycle **78** that in the presence of arynes lead to the anthracene products.[263,264]

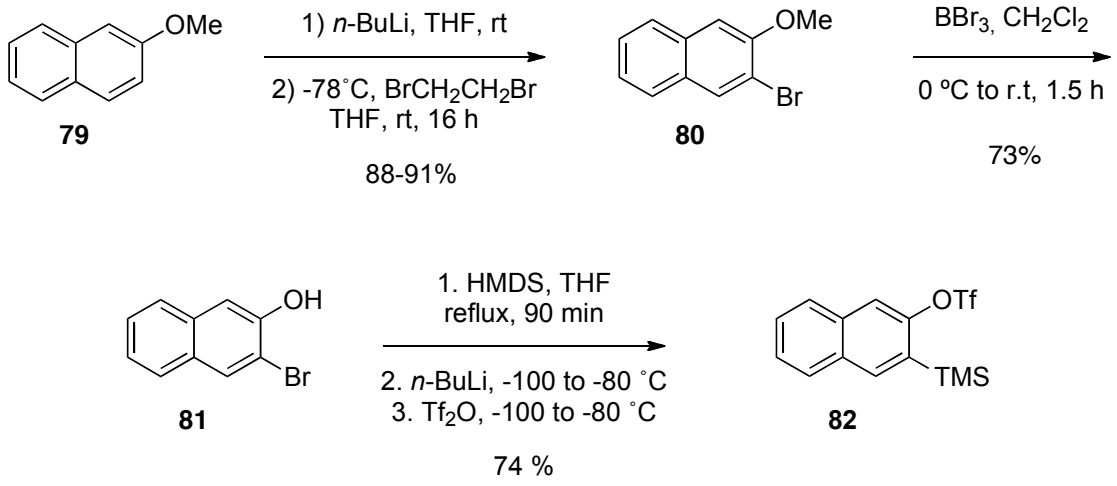


Scheme 89

3.4.2 Development of the Second Strategy

Our first aim was to apply this methodology in the synthesis of C_3-symmetric heptastarphene-(2.2.2), **73**. Starting from commercially available 2-

methoxynaphthalene (**79**), *ortho*-bromination,[265] followed by treatment with BBr_3, furnished 2-hydroxy-3-bromonaphthalene (**81**) in good yields (*Scheme 90*). Following an improved procedure for the synthesis of *ortho*-silylaryltriflates,[266] *ortho*-bromonaphtol was transformed to the desired 2,3-disubstituted naphthalene **82** in 78% yield.



Scheme 90

3.4.2.1 Synthesis of Trinaphthylene

Under the described procedure for the palladium-catalyzed [2+2+2]-cyclotrimerization reaction of arynes,[261] naphthalyne precursor **82** gave the desired trinaphthylene **73** in 41% yield (*Scheme 91*). Due to the insolubility of the compound, purification could not be achieved by column chromatography or recrystallization, and its isolation was performed by filtration and washing with several organic solvents.

265 Laufer, R. S.; Dmitrienko, G. I. *J. Am. Chem. Soc.* **2002**, *124*, 854-1855.

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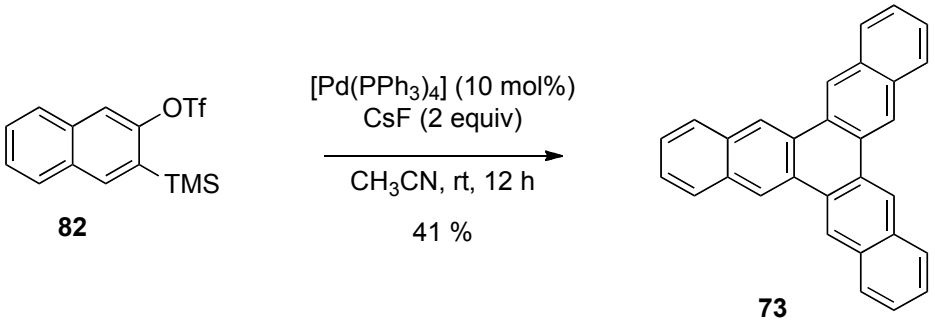

82 **73**

Scheme 91

Trinaphthylene **73** was deposited on NaCl insulating layer and on a gold surface and STM imaged at low temperature (see section 4.3).[10]

3.4.2.2 Synthesis of Starphene Derivatives with C_2-Symmetry

Our next aim was to apply the palladium-catalyzed [2+2+2]-cocyclotrimerization between arynes and dimethyl acetylenedicarboxylate (DMAD) to obtain the corresponding 9,10-dicarboxyphenanthrene (**83**) and 1,2,3,4-tetracarboxy-anthracene (**84**) (see *Scheme 92*).

For the synthesis of 9,10-dicarboxypentaphene (**83**) under the reported conditions,[267] when $[Pd(PPh_3)_4]$ was used as the catalyst, and 1.4 equiv of DMAD were added, an approximately 1:1 mixture of pentaphene **83** and anthracene **84** derivatives was obtained. However, when 1.2 equiv of DMAD were used, with $Pd(OAc)_2$ and PPh_3 as catalytic system, only the pentaphene **83** although the isolated yield was low (*Scheme 92*). Moreover, using $[Pd_2(dba)_3 \cdot dba]$ and 5 equiv of DMAD,[266] anthracene product **84** was obtained in 66 % yield.

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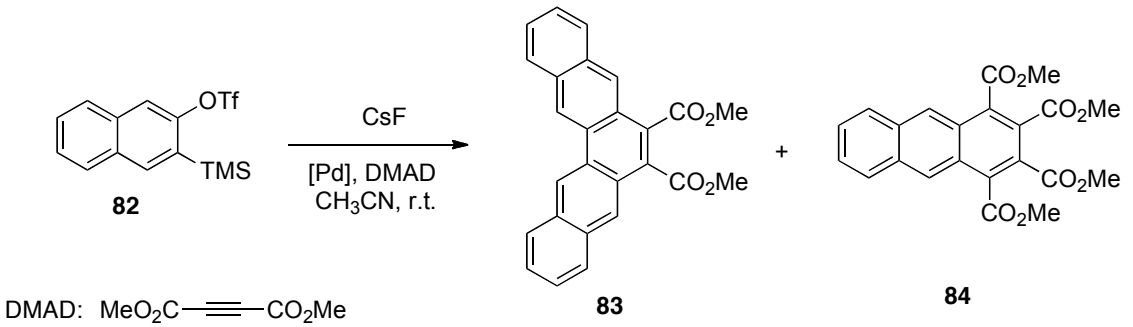

Conditions: $[Pd(PPh_3)_4]$ (10 mol%), DMAD (1.4 equiv); **40% 83 + 34% 84**
$[Pd(OAc)_2]$ (10 mol%), PPh_3 (20 mol%), DMAD (1.2 equiv); **20 to 50% 83**
$[Pd_2(dba)_3 \cdot dba]$ (10 mol%), DMAD (5 equiv); **66 % 84**

Scheme 92

Having into account some of the precedents in the literature for the preparation of acenes, we decided to transform compounds **83** and **84** to the corresponding bromomethyl derivatives. These may serve as staring material from which different methodologies could be applied for the ring extension of one or two of the branches. For instance, following Takahashi's procedure for the alkynylation of *ortho*-dribromo methyl groups and coupling reaction via zirconocene intermediate with 1,2-diiodobenzne, extension of the branches, containing a six member non-aromatic ring, could be performed. On the other hand, a [4+2]-cycloaddition reaction with quinone via formation of *ortho*-quinodimethene following Cava's reaction, would give compounds with extended branches containing quinones that could be further functionalized.

Reduction of the dimethylcarboxylate **83** to the corresponding diol **85** that, without further purification, was treated with PBr_3 to give the desired 6,7-bis(bromomethyl)pentaphene **86**. However, the insolubility of the dihydroxy intermediate **85** and the dibromo product **86** made purification difficult, and only milligram quantities of dibrominated adduct could be obtained (*Scheme 93*).

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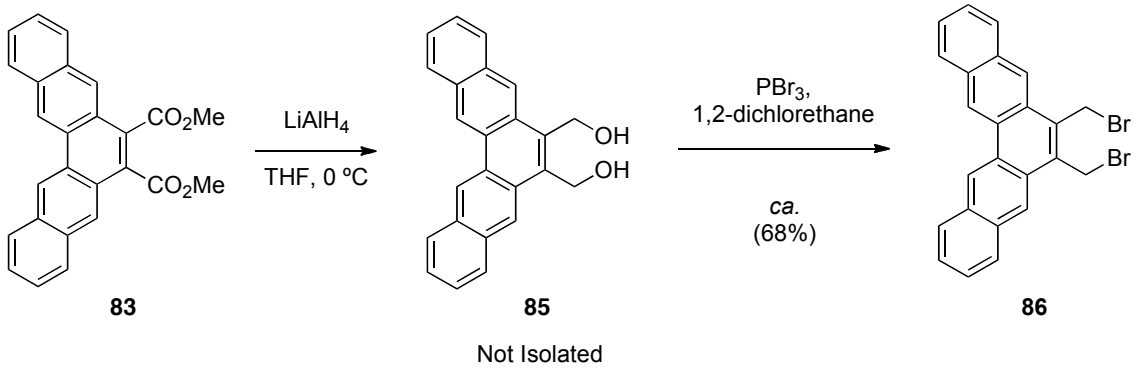
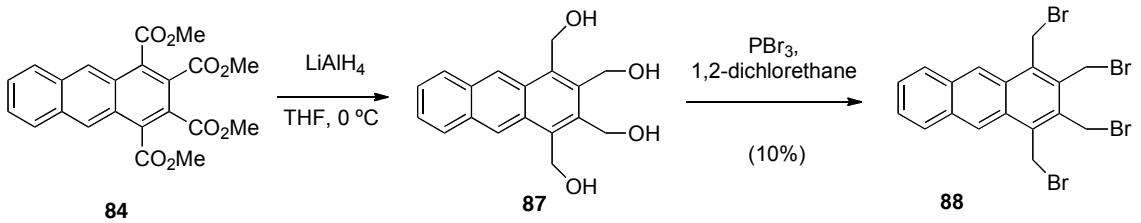


83 **85** **86**

Not Isolated

Scheme 93

Tetramethyl anthracene 1,2,3,4-tetracarboxylate (**84**) could similarly be transformed into 1,2,3,4-tetrakis(bromomethyl)anthracene compound (**88**) in low yields (10% yield for two steps) (*Scheme 94*).



84 **87** **88**

Not isolated

Scheme 94

Branch extension was first attempted by applying the methodology reported by Takahashi and co-workers.[268] However, alkynylation of 6,7-bis(bromomethyl)pentaphene (**86**) and 1,2,3,4-tetrakis(bromomethyl)anthracene (**88**) with 1-pentyne in the presence of *n*-BuLi furnished in both cases in a complex mixture from which the desired products could not be isolated (*Scheme 95*).

268 Takahashi, T.; Kashima, K.; Li, S.; Nakajima, K.; Kanno, K. *J. Am. Chem. Soc*. **2007**, *129*,

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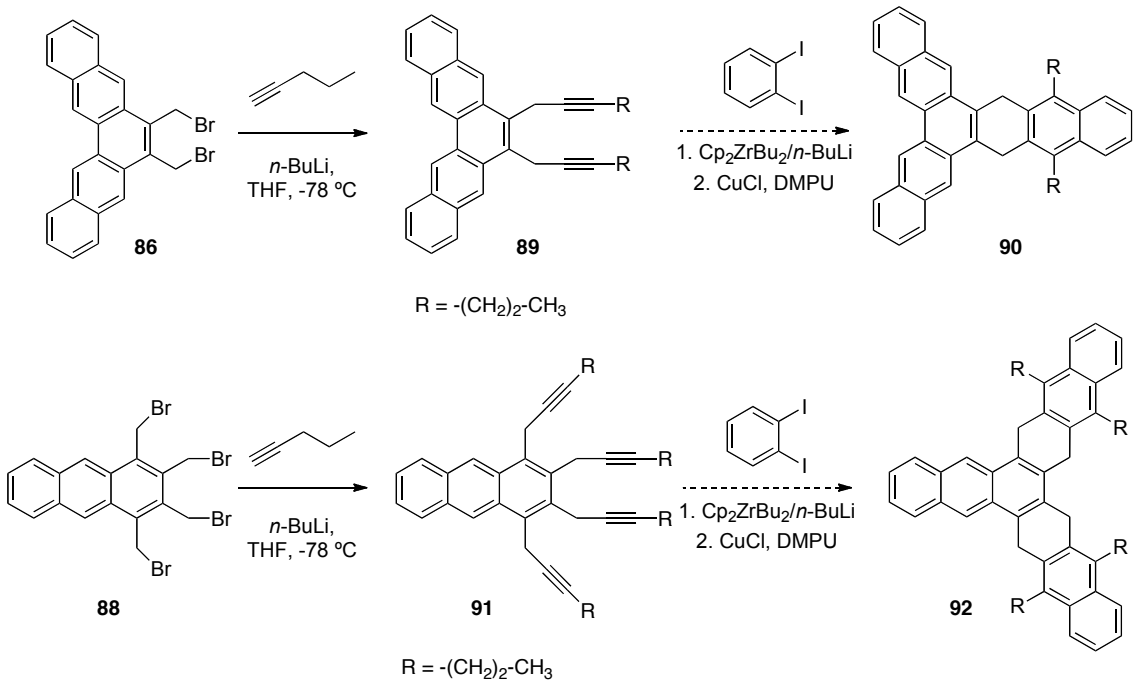
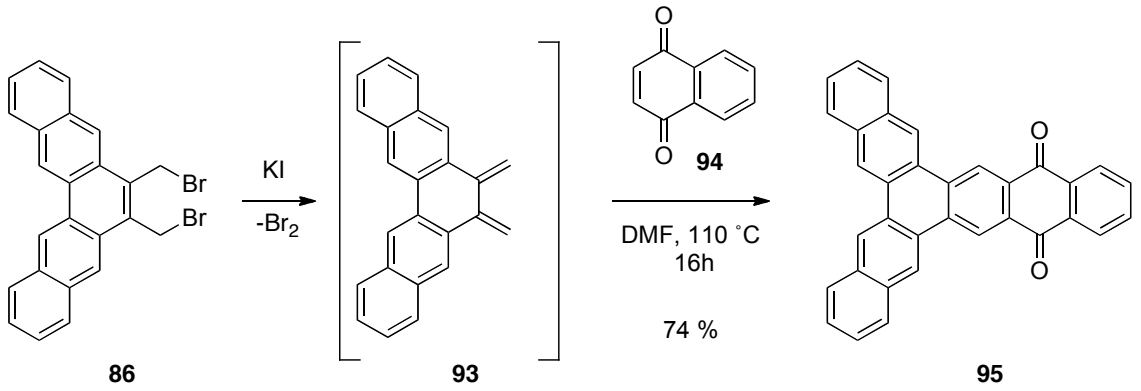


Scheme 95

Besides, we applied Cava's reaction[228,229] on compound **86** in the presence of KI, via *ortho*-quinodimethene **93**, gave benzo[*b*]trinaphthylene-13,18-dione (**95**) in 74% yield (*Scheme 96*).



Scheme 96

Having shown that heptastarphene-(2.2.2) **73** without any anchoring groups could be deposited and imaged by STM on insulating and gold-metal surface (see Chapt 4.3) we decided to reduce quinone **95** to obtain octastarphene-(2.2.3) **96**. However, reduction of **95** with $LiAlH_4$ and subsequent dehydration with HCl, following a four-step procedure, gave a mixture of products (probably different hydroxy

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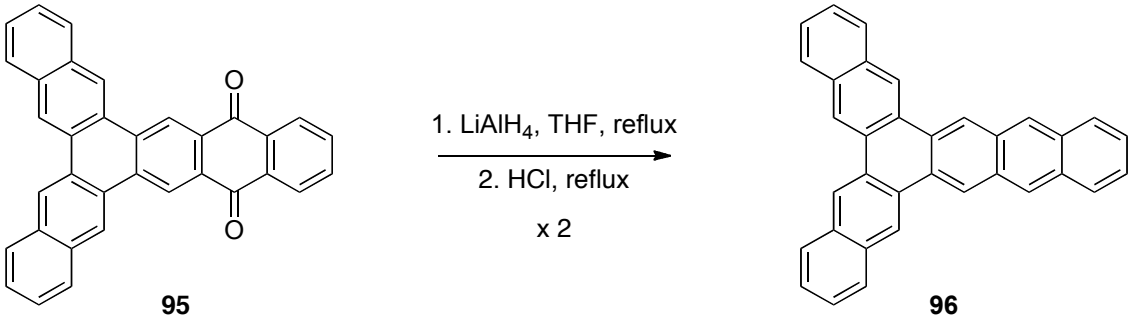
intermediates and the desired product). Due to its poor solubility, the starphene **96** could not be isolated and purified by column chromatography (*Scheme 97*).



95 **96**

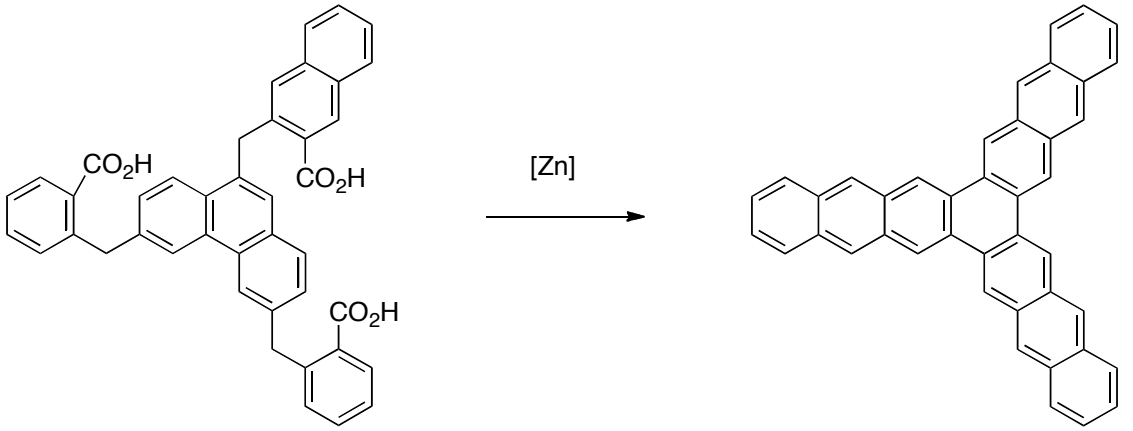
Scheme 97

3.5 Deacastarphene-(3.3.3)[269]

We wanted to synthesize decastarphene-(3.3.3) **97** with three anthracenic branches. An additional benzene-unit on the branches will mean an additional node in their molecular orbitals, which should have an important influence on the electron transfer process observed by STM techniques. In addition, comparison of experimental STM results between trinaphtylene and its higher homologue decastarphene would be of great interest.

Two different methodologies have been reported for the synthesis of decastarphene-(3.3.3) **97**. The first one, developed by Clar and Muller,[205] is based on the synthesis of triacid **98** that, in the presence of Zinc salts and Zinc dust, undergoes a Friedel-Crafts three-fold cyclization reaction to give starphene **97** (*Scheme 98*). However, no yield was reported for the cyclization, drastic conditions were required and only an analytical pure sample of **97** could be isolated.

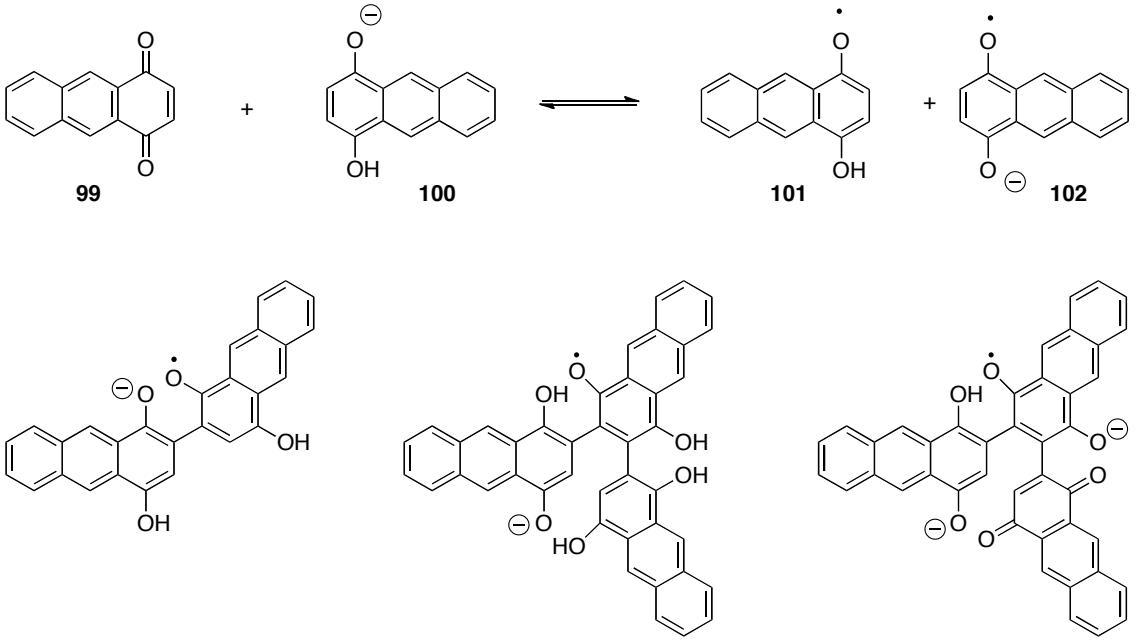
269 The synthesis of decastraphene-(3.3.3) was carried out in collaboration with Dr. Thorsten



98 **97**

Scheme 98

Brockmann and Laatsch reported an alternative procedure for the synthesis of decastarphene based on the trimerization of quinones[270] via an anionic-radical mechanism. According to the authors, in basic media, substoichiometric amounts of anion **100** can react with anthraquinone to give two radical species, **101** and **102**, that are in equilibrium with the starting material. In the presence of an excess of quinone, both intermediates can react to form the radical/anion intermediates proposed in *Scheme 99* that will finally deliver the desired trimerized anthraquinone.



99 **100** **101** **102**

Scheme 99

270 Brockmann H.; Laatsch, H. *Chem. Ber.* **1973**, *106*, 2058-2069.

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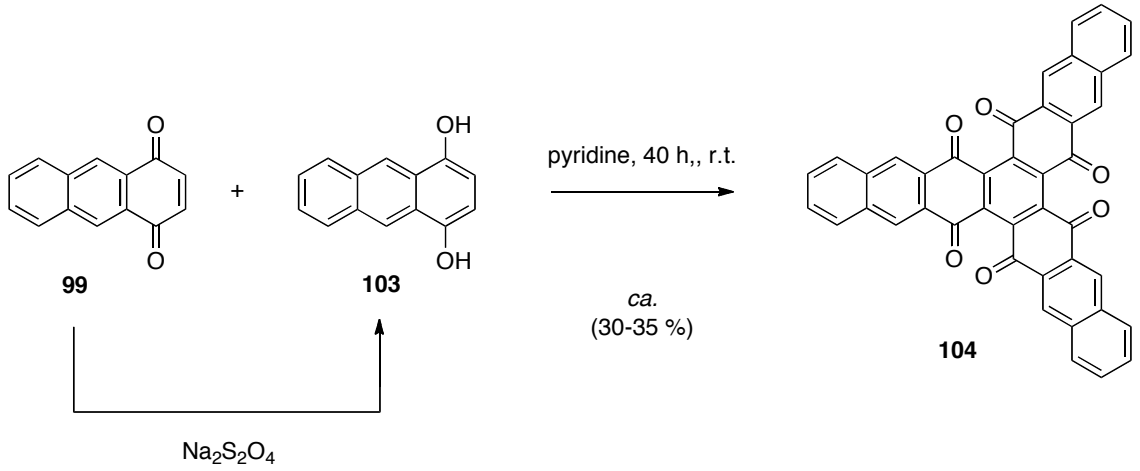
Following this last procedure, trimerization of 1,4-anthraquinone (**99**) took place in pyridine in the presence of freshly prepared 1,4-dihydroxyanthracene (**103**) by reducing in situ small amounts of anthraquinone **99**. Under the reaction conditions, a complex mixture of insoluble products precipitated from the crude mixture. After filtration and several washings with different common organic solvents, trianthraquinone **104** was obtained in *ca*. 30 to 35% yield, as a green insoluble solid that could only be characterized by NMR at 130 ºC in 1,1,2,2-tetrachloroethane-d_2. Due to the high insolubility of this compound and difficulties on its characterization, compound **104** was used on the next step without further purification.



Scheme 100

For the reduction of trianthraquinone **104**, several methods reported in the literature were applied. When alumminium-amalgam in cyclohexanol was employed, a complex mixture of hydroxy intermediates was obtained and no pure product could be isolated. On the other hand, when BH_3·THF was used the presence of a reduced compound, containing dihydro-anthracenic branches, was detected by NMR. No pure compound could be isolated and all attempts to oxidize the crude mixture to give the fully aromatic starphene were unsuccessful. When $LiAlH_4$ was used as reducing agent in the presence of $AlCl_3$ or BF_3·OEt_2, again pure compound **97** could not be isolated from the crude mixture. The best results were obtained when the reduction/dehydration sequence was applied with $LiAlH_4$ and HCl. Thus under the fourth-step procedure, desired [3.3.3]-decastarphene **109** was isolated in 18 % yield

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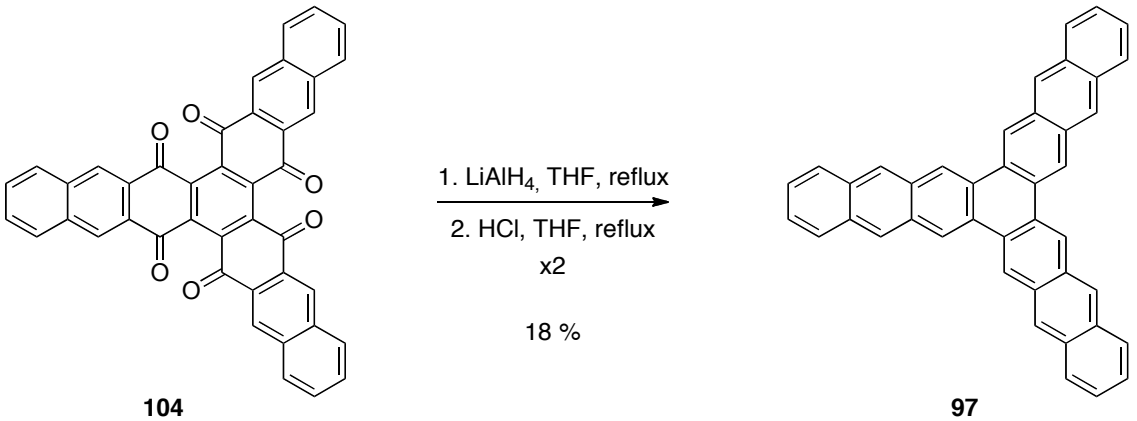
in more than 95 % purity according to ^{1}H NMR (130 ºC in 1,1,2,2-tetrachloroethane-d_2).



104 **97** $C_{42}H_{24}$

Scheme 101

In addition, according to a modified procedure described by Brockmann and Laatsch,[270] a second successful procedure for the reduction of anthraquinone was performed. Thus, by using drastic conditions early reported by Harvey and co-workers,[271] with red phosphotus and HI (60%) at 200 ºC, reduction of the central aromatic ring of anthracene branches was observed in the crude mixture in 80% yield (*Scheme 102*). As already described,[270] a 1,3-shift of hydrogen from the reduced quinone ring to the central ring of the anthracene system occurred and was confirmed by 2D ^{1}H NM at 130 ºC in 1,1,2,2-tetrachloroethane-d_2. Intermediate **105** was purified by recrystallization. A aromatization to obtain the desired starphene **97** could be achieved with chloranil in 10% isolated yield or by dehyrogenation in the presence of Pd/C in a 8% yield of 80% pure decastarphene-(3.3.3) **97** based on ^{1}H NMR analysis (130 ºC in 1,1,2,2-tetrachloroethane-d_2).

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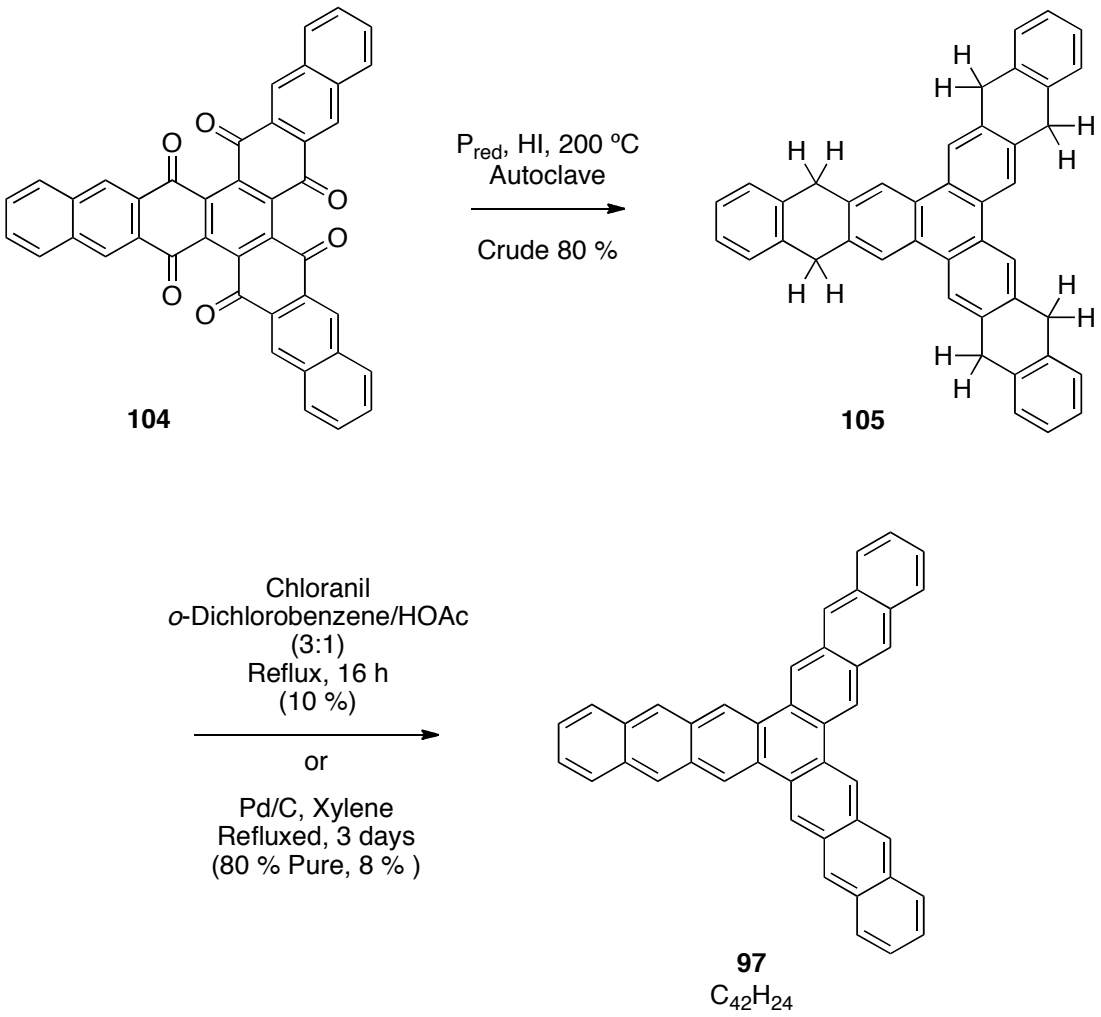

Scheme 102

Decastarphene molecule has been deposited on a on 2NaCl/Cu(111) surface and LT-UHV STM experimental images have been obtained for single molecules (see additional information on Section 4.4)[10] while hexahydrostarphene **105** is also under current studies.

3.6 Aza Polyaromatic Analogues

For our purposes on the investigation of the electron current transport through single molecules and their future implementation on molecular electronic devices, aromatic nitrogen-containing heterocycles substituting one or more of the benzyl units are of high interest.

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3.6.1 Phenanthroline Derivatives

Initially, we wanted to explore the influence of nitrogen atoms on surface deposition, as well as its coordination to metal atoms on surfaces. Phenanthroline derivatives with two pyridine moieties have been widely employed as bidentate coordinated ligands with many different metals. Our plan was to prepare aromatic extended phenanthrolines that could act as molecular wires. Aromatic branches could be functionalized to connect them with circuitry molecules, while nitrogen atoms could coordinate to atomic metal wires (*Figure 44*).

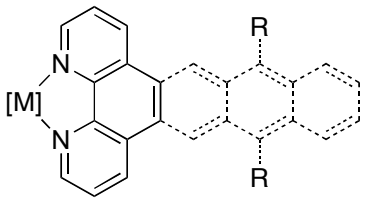
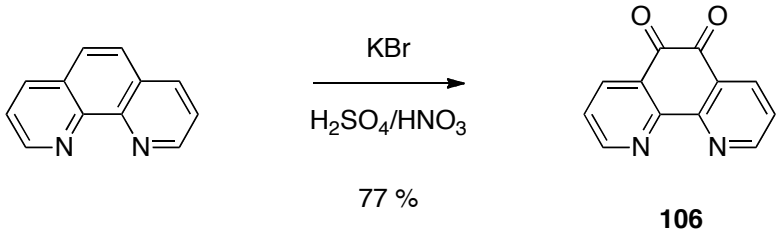


Figure 44: Aromatic extended phenanthrolines where nitrogen atoms can coordinate to metals.

To access to a variety of extended phenanthrolines, we initially oxidized phenthroline to obtain 9,10-phenanthroline-5,6-dione (**106**) (*Scheme 103*) that could be further coupled with several *ortho*-substituted acenes.



Scheme 103

As model systems, we followed reported procedures for the condensation of phenenthrolinedione **106** with two different substituted benzenes: 2,2'-(1,2-phenylene)diacetonitrile,[272] and benzene-1,2-diamine[273] as shown in *Scheme 104*.

272 Albano, G.; Belser, P.; De Cola, L.; Gandolfi, M. T. *Chem. Commun.***1999**,1171-1172.

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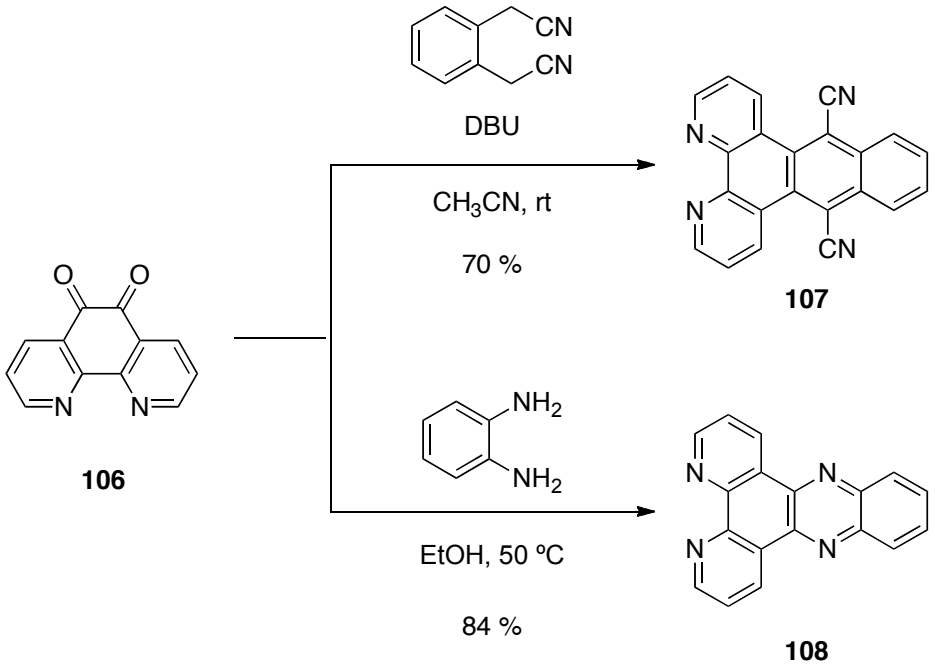
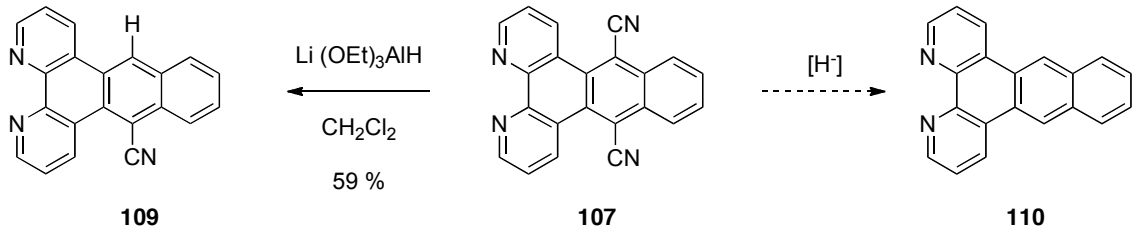
These reactions could be further extended via condensation with disubstituted naphthalene or higher acene homologues.



Scheme 104

For preliminary experimental studies on the STM manipulation for nitrogen-metal coordination on surfaces, we also wanted to prepare the naphthalene model system **110**. Thus, starting with compound **107** we employed several alumminium hydrides ($LiAlH_4$, DIBAL, $Li(OEt)_3AlH$) as reducing agents. Reduction of one of the cyano groups to give compound **109** could be achieved when $Li(OEt)_3AlH$ was used,[274] while no reduction at all was observed when the other reducing reagents were employed.



Scheme 105

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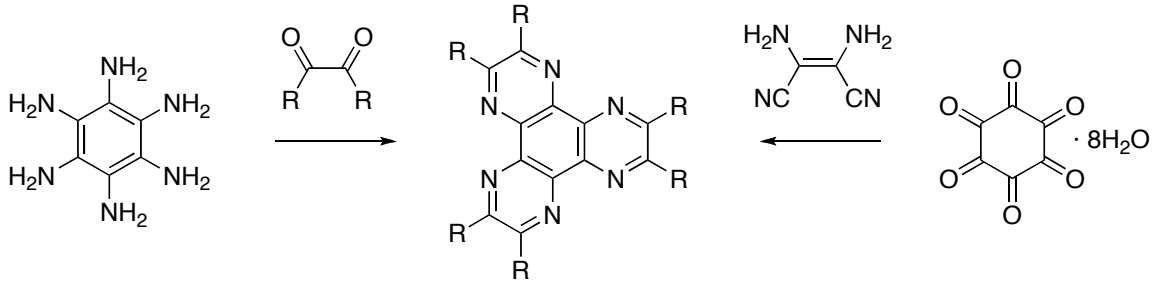
Preliminary STM studies of naphtho[2,3-*f*][1,10]phenanthroline-9-carbonitrile (**109**) on a NaCl insulating surface have been performed (see Section 4.5).[10]

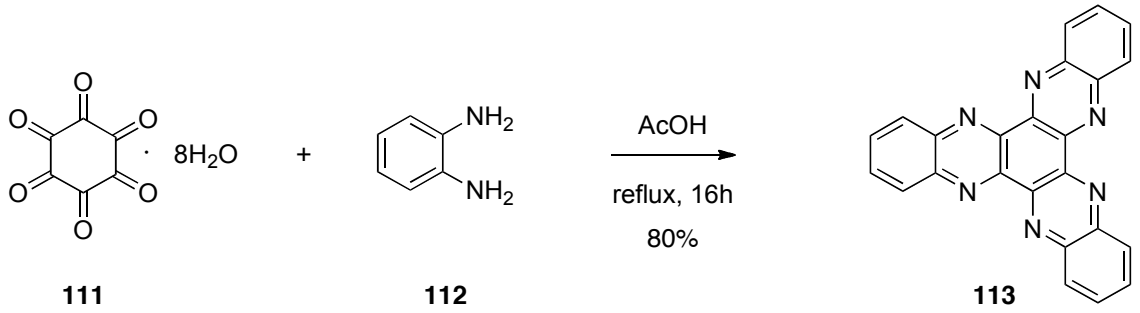
3.6.2 Azastarphenes

The synthesis of azatriphenylenes has already been reported employing Hinsberg condensation between hexaaminobenzene and 1,2-dicarbonyl derivatives[218] or between hexaketocyclohexane and 1,2-diamino derivatives as shown in *Scheme 106*.[219]



Scheme 106

In our case, for the synthesis of diquinoxalino[2,3-*a*:2',3'-*c*]phenazine (**113**), we carried out the condensation between commercially available hexacycloketone (**111**) and 1,2-diaminobenzene (**112**). Due to its higher solubility compared to its carbon analogue, azatrinaphthylene **113** could be purified and isolated by recrystallization in 80% yield (*Scheme 107*).



111 **112** **113**

Scheme 107

Similarly, condensation between hexacycloketone (**111**) and 2,3-diaminonaphthalene (**114**) followed by recrystallization gave the desired azastarphene homologue **115** in very good yields (83%) (*Scheme 108*).

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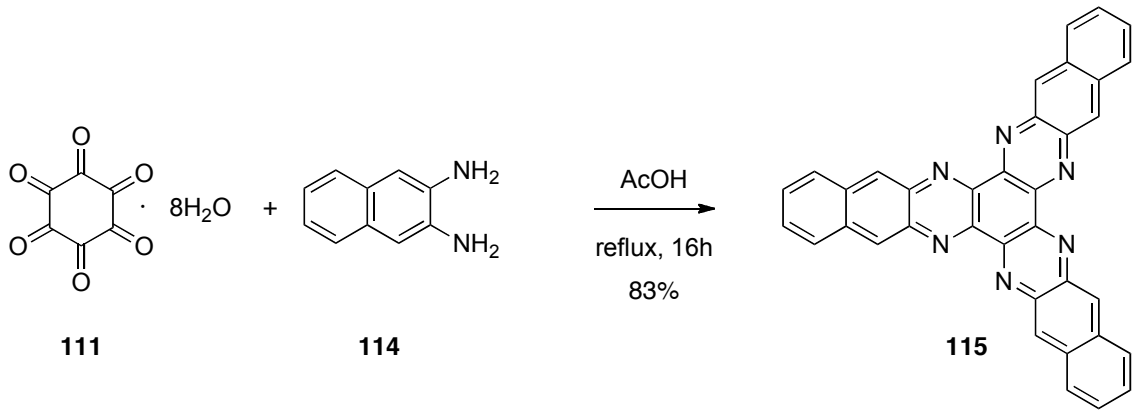

111 **114** **115**

Scheme 108

Both azastarphenes, **113** and **115**, are currently being studied by STM.[10]

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4. Applications

In collaboration with Pico-Inside partners, some of the molecules synthesized have been deposited on different isolating and metallic surface and have been imaged and manipulated by means of STM or AFM.

4.1 STM and NC-AFM Studies on Tribenzyltruxenes

4.1.1 *syn*-5,10,15- Tribenzyltruxene (2b)[275]

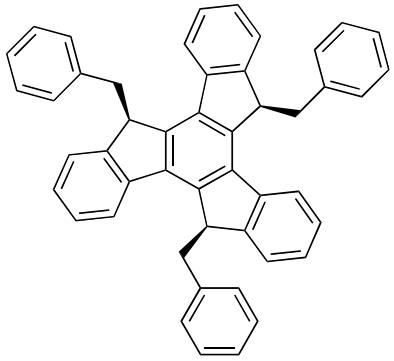

*Figure 45: syn-5,10,15- Tribenzyltruxene **2b**.*

syn-Truxene **2b** has been vapor-deposited on top of a NaCl insulator layer on a Cu(111) surface at 4.5 K (*Figure 43*). Although STM images were complex, single molecules *(Figure 43a)* adopting several conformations when deposited upon the surface have been imaged *(Figure 43b)*. For instance, some molecules present an extended central lobe, like shown in *Figure 43c*, while others present a bright lobe in one side of the molecule (*Figure 43d*).

275 STM experimetal studies have been carried out by Christian Joachim research group at the

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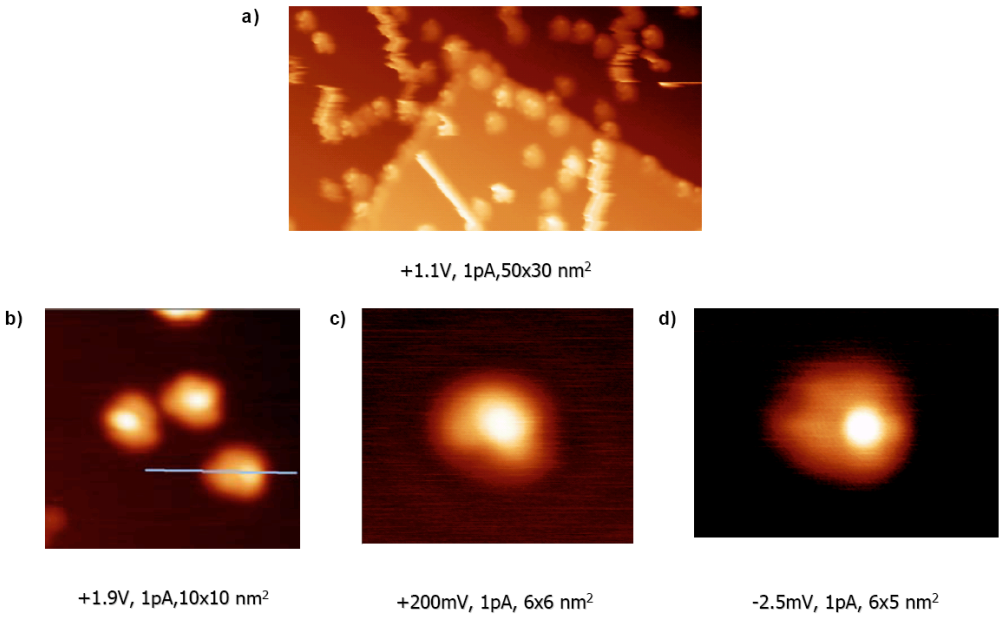

Figure 46: STM images of various conformations for syn-5,10,15- tribenzyltruxene at different scale and with different experimental conditions.

Further experiments showed that **2b** molecules can be manipulated with the tip appendix of the STM and that the internal structure can also be modified by variation of the voltage parameter (*Figure 47*).

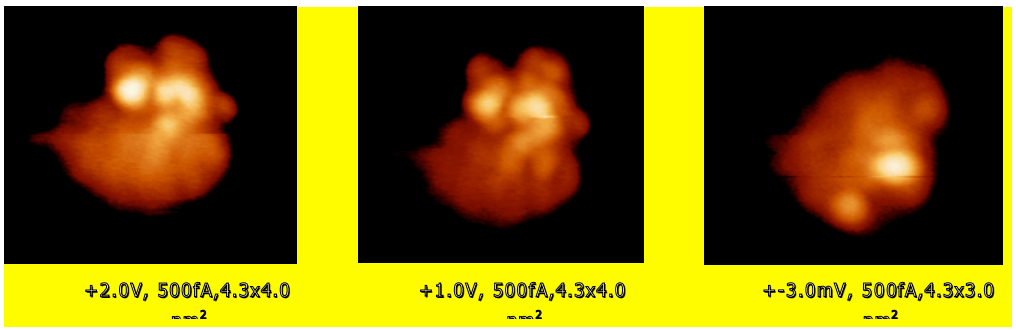

Figure 47: STM images of internal electronic structure manipulation.

Simple calculations for STM theoretical images were also carried out using the Elastic Scattering Quantum Chemistry (ESQC)[166] technique. As shown in *Figure 48*, similar experimental and calculated STM images show a good correlation between calculated and experimental data (*Figure 9*).

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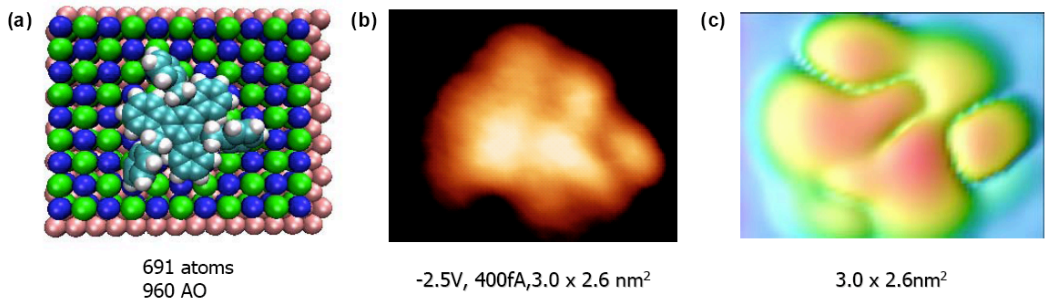
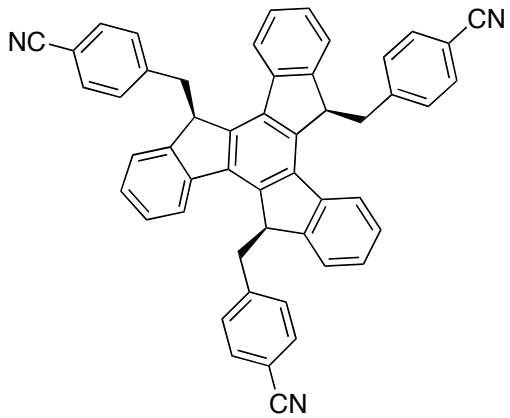


Figure 48: (a) CPK model of syn-tribenzyltruxene deposited on a NaCl layer (b) experimental and (c) theoretical calculations of STM image.

These results with the simple model system have demonstrated that truxene derivatives can be imaged and manipulated with STM. Nevertheless, as stated, the high mobility and conformational freedom of *syn*-benzyltruxene on insulating surface, difficults its manipulation and furthermore its applicability in electronic devices.

4.1.2 *syn*-Tris(4-cyanobenzyl)truxene (3a)[276]



3a

*Figure 49: syn-Tris(4-cyanobenzyl)truxene **3a**.*

276 NC-AFM studies have been developed by Enrnst Meyer and co-workers from the Department of Physics at the University of Basel, while atomistic simulations have been carried out by Thomas Trevethan and co-workers at the Department of Physics and Astronomy from the University College London. As a result of these work the next publication has been accepted in *ACS Nano* magazine: B. Such, T. Trevethan, T. Glatzel, S. Kawai, L. Zimmerli, E. Meyer, A. L. Shluger, C. H. M. Amijs, P. de Mendoza, and A. M. Echavarren; *Functionalized organic molecules: Adsorption and diffusion of single molecules on the KBr surface*, nn-2010-00424g.

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syn-5,10,15-Tris(4-cyanophenylmethyl)truxene **3a** molecules were adsorbed onto patterned KBr (001) surface. At low coverages, single molecules have been imaged with atomic and molecular resolution with the NC-AFM at room temperature. The images obtained show that individual molecules are immobilized on monolayer kink sites of the terraces while molecules are observed rapidly diffusing along the perfect monolayer step edges. Extensive atomistic simulations have been performed on this system to understand the mechanisms of adsorption and diffusion of the molecule on the different surface features. According to theoretical modeling calculations, interaction of the truxene molecule with the surface is dominated by polar CN groups of the benzonitrile substituent since benzonitrile molecule adsorb above K^+ ion sites in the surface (*Figure 50*).

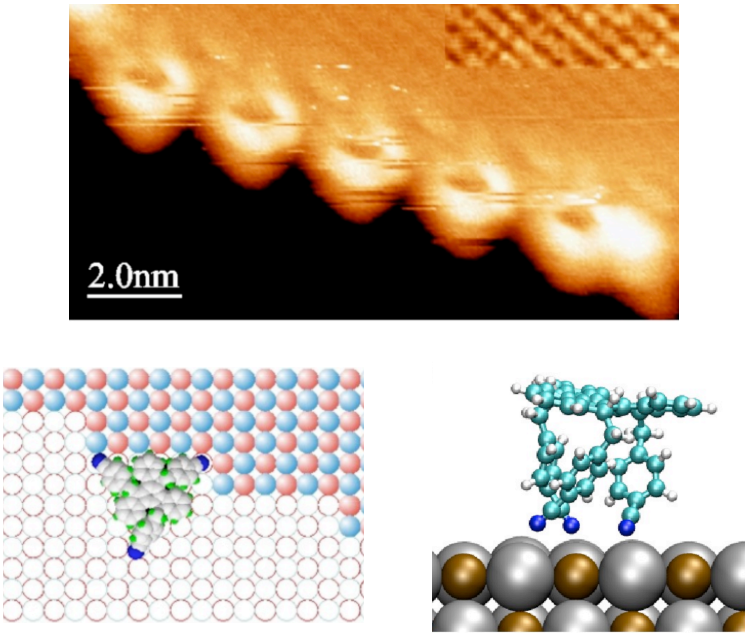

Figure 50: (a) NC-AFM image of truxene X adsorbed on the KBr step edges at room temperature with (b) the proposed configuration of the imaged step and (c) theoretical modeling, showing the three flexible cyanobenzyl groups anchoring on the surface.

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4.2 STM studies of Starphenes

4.2.1 Trinaphthylene (73)[275]

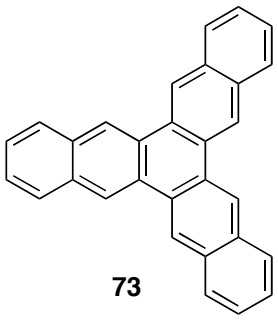

*Figure 51: Trinaphthylene **73**.*

Trinaphthylene **73** has been deposited on metallic Cu(111) surface and LT-UHV-STM experimental images have been obtained (*Figure 52*).

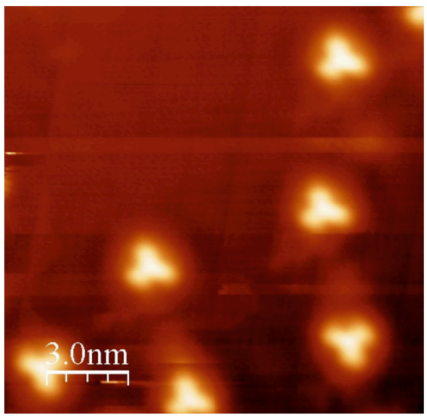

*Figure 52: LT-UHV-STM experimental images of trinaphtylene **73** on Cu(111) surface at T = 4.8 K*

When trinaphthylene molecules have been deposited on a bilayer 2NaCl/Cu(111) the HOMO and LUMO orbitals have been imaged showing the agreement between experimental and theoretically ESQC images (*Figure 53*).

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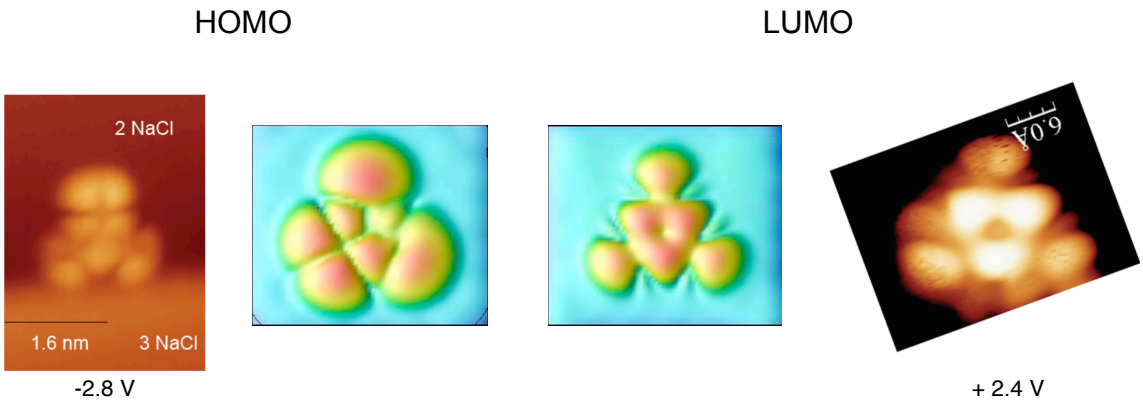

*Figure 53: LT-UHV-STM experimental and theoretical images of trinaphtylene **73** HOMO and LUMO orbitals on 2NaCl/Cu(111) surface at T = 4.8 K*

Furthermore, after manipulation with Au atoms, trinaphthylene molecules have served to prepare a functional molecular logic gate. Thus, Au atoms have been manipulated with the tip of the STM towards the two naphthyl branches of a single trinaphthylene molecule adsorbed on a Au(111) surface. One Au atom brought in contact with the molecule acts as one bit of classical information input on the molecule. The molecular π-orbital system converts this input in quantum information available all over the trinaphthylene molecular board. The Au-trinaphthylene electronic interactions give rise to molecular orbitals splitting and measurable energy shifts revealing the trinaphthylene functionality as a *NOR* logic gate (*Figure 54*).

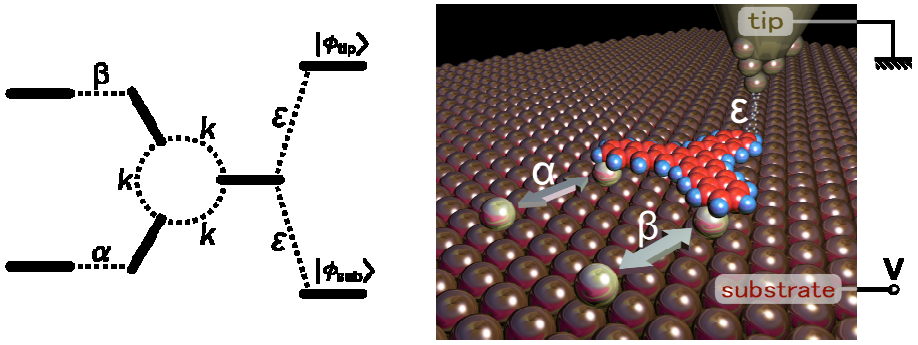

*Figure 54: Schematic representation trinaphthylene molecule **73** with two gold atoms as NOR logic gate.*

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This *NOR* function has been characterized by means of tunnelling spectroscopy and by imaging the corresponding molecular electronic state displacements using dI/dV constant current mapping (*Figure 55*).[277]

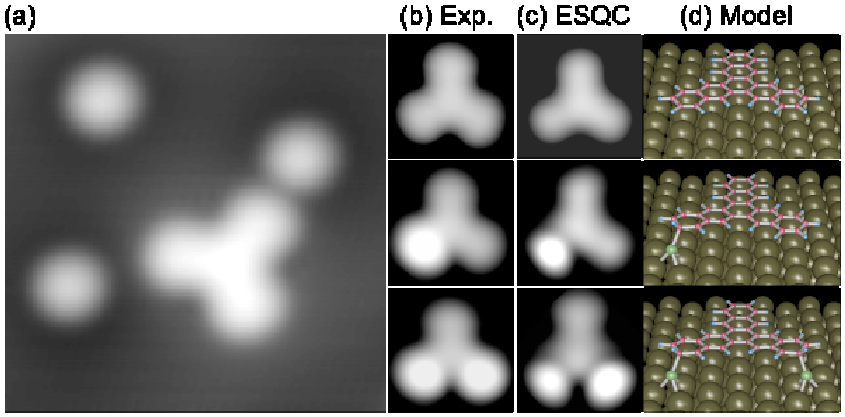

*Figure 55: Experimental and theoretical topographic images of trinaphthylene molecule **73** with 0, 1, and 2 Au atoms.*

These results are an interesting example for the use of inherent quantum properties on the molecular level. This molecule presents the smallest complete logic gate ever synthesized.

4.2.2-Decastarphene-(3.3.3) (97)[275]

Decastarphene molecule **97** was also deposited on a on 2NaCl/Cu(111) surface. At T = 4.8 K, STM experimental images have been obtained for the HOMO-LUMO gap of the molecule (*Figure 56*).

277 Theoretical and STM experiments have been carried out in the group of Joachim at the CNRS and the group of Soe in Singapore. The results of this work have been submitted for publication: W. H. Soe, C. Manzano, N. Renaud, P. de Mendoza, A. De Sarkar, F. Ample, M. Hliwa, A. M. Echavarren, N. Chandrasekhar and C. Joachim, *A Single Molecule NOR*

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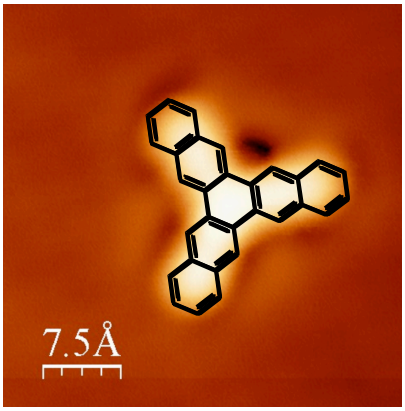

*Figure 56: LT-UHV-STM experimental image of decastraphene **97** HOMO/LUMO gap.*

In addition, the HOMO and LUMO orbitals have been also experimentally imaged and the results are in agreement with the theoretically ESQC calculated ones (*Figure 57*). Together with the calculations on trinaphtylene and their experimental images these new results could validate ESQC as an appropriate tool to predict electronic properties for these systems.

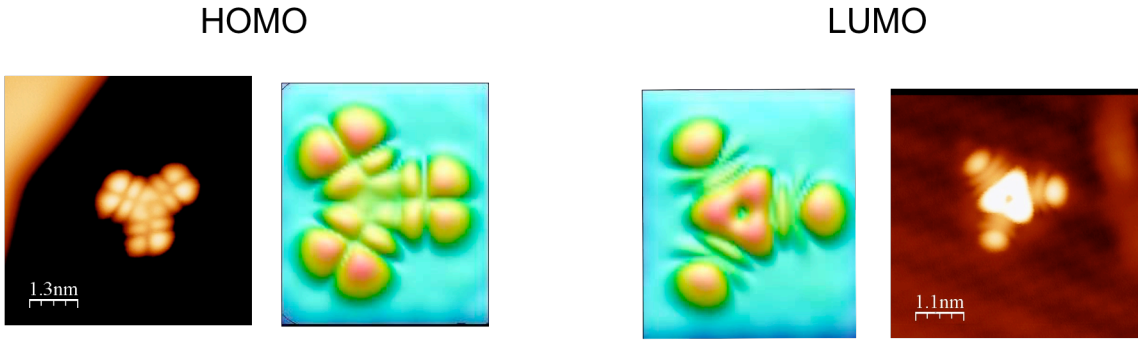

*Figure 57: LT-UHV-STM experimental and theoretical images of decastraphene **97** HOMO and LUMO orbitals on 2NaCl/Cu(111) surface at T = 4.8 K*

Studies on the manipulation of decastraphene and gold atoms to assess logic functionality to the molecule are currently in progress. The azastarphenes analogues **113** and **115** are currently under investigation.

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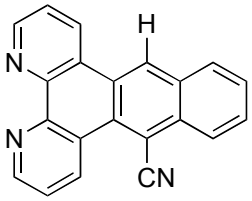
4.3 Aza-polyaromatic Systems

4.3.1 Naphtho[2,3-*f*][1,10]phenanthroline-9-carbonitrile (109)[275]



109

*Figure 58: Naphtho[2,3-f][1,10]phenanthroline-9-carbonitrile (**109**)*

Finally, the simplest polyaromatic derivative containing nitrogen atoms that could coordinate to metal atoms, phenanthroline **109**, has been investigated on surface deposition. Preliminary studies show that orbital-like LUMO images can be obtained. Further ongoing experiments are focused in the co-adsorption of gold atoms and the molecules and to induce the reaction between these two species either thermically, by heating the sample, or by lateral manipulation of the molecules.

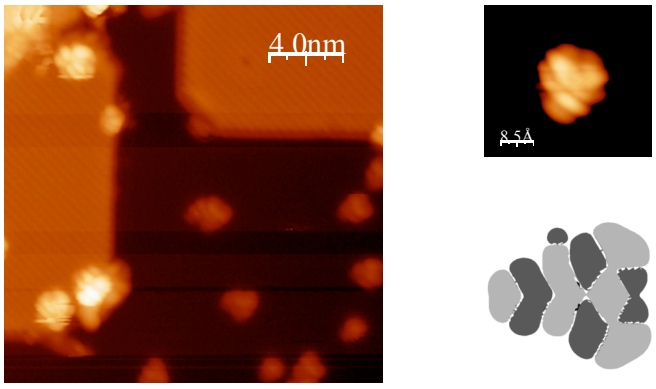


*Figure 59: Large scale image of the phenanthroline derivative **109** on 3 and 2 layers of NaCl on Cu(111). Top right: zoom on one of the molecule, bottom right: LUMO of the free molecule.*

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5. Conclusions

We have prepared *syn*-5,10,15-tribenzyltruxene as model system to investigate the quantum behavior of this family of C_3-symmetric non-alternant polyaromatic compounds on insulating surfaces and submitted it to STM studies. Besides obtaining interesting results on the imaging and even manipulation of the molecule with the tip of the STM, it turned out that this truxene is highly mobile on the surface. We designed related systems with anchoring groups. *syn*-5,10,15-Tris-(4-cyanophenylmethyl)truxene and *syn*-5,10,15-tris- (3-cyanophenylmethyl)truxene bearing cyano benzyl as anchoring groups and *syn*-tris(acridin-2-ylmethyl)truxene with benz[*a*]anthracene as pendant anchoring groups were successfully synthesized. Preliminary results on *syn*-5,10,15-tris(4-cyanophenylmethyl)truxene confirmed our strategy of immobilization and has allow to carry out a detail study of molecular dynamics at the nano-scale.

We have synthesized several fully conjugated Y-shaped molecules We developed a straightforward and effective access by microwave cross-coupling followed by photochemical reaction for the synthesis of helicenes.

In addition, we have applied palladium-catalyzed [2+2+2]-(co)-cyclotrimerization reaction of arynes for the synthesis of starphenes. Applying this methodology, we prepared *C3*-symmetric trinaphtylene and submitted it to STM electronic studies. Unprecedented, it could be demonstrated that in the atomic scale where quantum laws govern, trinaphthylene combined with single gold atoms can act as a *NOR* logic gate.

With these auspicious results in hands, we focused on higher homologue decastarphene-(3.3.3) containing an additional node that could be of profit during electron transfer processes. We optimized the synthesis of decastarphene to get a reliable access to the molecule, and to its also highly interesting derivative hexahydrodecastarphene-(3.3.3) with a break of conjugation in every of its three

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electronic properties studies. While experimental STM images of the frontier molecular orbitals of decastarphene and trinaphthylene are confirming the accuracy of ESQC calculations, STM studies on the electronic transfer process are crucial in order to support quantum Hamiltonian computing as a reliable modern theory for calculating the electronic processes inside a single molecule.

Furthermore, we employed the Hinsberg condensation for the synthesis of nitrogen-containing azastarphenes, which have different but also interesting properties compare to its carbon analogues. We have synthesized diquinoxalino[2,3-*a*:2',3'-*c*]phenazine as azaderivative of trinaphtalene and its higher analogue of aza-decastarphene.

Finally we prepared model systems containing phenthroline subunits as molecular hooks able to coordinate to metal atoms acting as molecular wires. Developing a modular strategy for their preparation, we have synthesized four different examples of these interesting systems. Studies on their suitability are still ongoing.

Compendiously, we developed several methodologies for the preparation of molecules with potential applications in molecular electronics and applied them in the synthesis of potentially candidates for this purpose. Even if the investigations by physico-chemical methods by our collaboration partners are still ongoing, the preliminary results show that we made a substantial contribution to verify computational methods relevant in this field. Furthermore, we obtained already pioneering and unprecedented results on the usage of our designed molecular devices.

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Chapter II:

Experimental Section

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Methods

All reactions were carried out under N_2 or Ar. Solvents were dried using a Solvent Purification System (SPS) or using standard procedures,[278] except for dimethylacetamide that was purchased anhydrous and packaged under N_2 (Aldrich). Analytical thin layer chromatography was carried out using TLC-aluminium sheets with 0.2 mm of silica gel (Merk GF_{234}). Flash chromatography purifications were carried out using flash grade Silica gel (SDS Chromatogel 60 ACC, 40-60 μm), Florisil (SDS, 60-100 mesh) or Alumina neutre (SDS, 0.063-0.2 mm, pH 6.3-7.7). NMR spectra (δ given in ppm) were recorded at 23 ºC on a Bruker Avance 400 Ultrashield (400 MHz for ^1H, and 100 MHz for ^{13}C) and at 130 ºC on a Bruker Avance 500 Ultrashield (500 MHz for ^1H) spectrometers at the *Institut Català d'Investigaciò Química (ICIQ)*. Mass spectra were recorded on a Waters Micromass LCT Premier (ESI) and Waters Micromass GCT (EI, CI) and Bruker Daltonics Autoflex (MALDI, LDI) spectrometers at the *ICIQ*.

1. Synthesis of Truxenes

The synthesis of *syn*-tribenzyltruxene **2b**, *syn*-cyanobenzyl truxenes **3a** and **3b** have already been described.[279] The synthesis of alkylating agents for the synthesis of truxenes 8 and 12, (bromomethyl)benz[*a*]anthracene[280,281] and 2-(bromomethyl)acridine **11** have already been described.[282,283]

278 (a) Burfield, D. R.; Lee, K.-H.; Smithers, R. H. *J. Org. Chem.* **1977**, *42*, 3060-3065. (b) Burfield, D. R.; Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 3966-3968. (c) Perrin, D. D.; Armarego, S. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon: New York, **1980**.

279 de Frutos, Ó.; Granier, T.; Gómez-Lor, B.; Jiménez-Barbero, J.; Monge, A.; Gutierrez-Puebla, E., Echavarren, A. M. *Chem. Eur. J.* **2002**, *8*, 2879.

280 Newman, M. S.; Gaertner, R. *J. Am. Chem. Soc.* **1950**, *72*, 264-273.

281 Sangaiah, R.; Gold, A.; Toney, G. E. *J. Org. Chem.* **1983**, *48*, 1632-1638.

282 Baum, J. S.; Condon, M. E.; Shook, D. A. *J. Org. Chem.* **1987**, *52*, 2983-2988.

283 Kitahara, Y.; Mizuno, T.; Kubo, A. *Tetrahedron* **2004**, *60*, 4283-4288.

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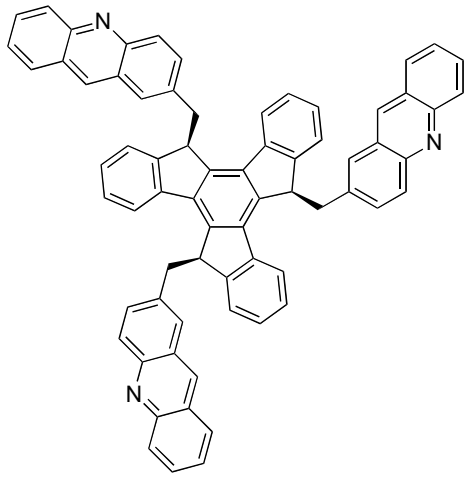
syn-Tris(acridin-2-ylmethyl)truxene (12b)



To a suspension of truxene **1** (100 mg, 0.29 mmol) in THF (10 mL) at -78 ºC was added *n*-BuLi (0.47 mL, 2.5 M in hexane, 4 equiv). The mixture was slowly warmed to -10 ºC over a period of 2 h and a solution of 2-(bromomethyl)acridine **11** (318 mg, 1.17 mmol) in THF (7 mL) was added dropwise. The resulting mixture was warmed to room temperature and stirred overnight. The reaction was quenched with NH_4Cl (aq) and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and evaporated in vacuum. Trituration with hexane yielded a yellow powder (mixture of *anti*/*syn* **12a** and **12b**). This mixture was suspended with *t*-BuOK (81 mg, 0.72 mmol) in *t*-BuOH (12 mL) and heated at reflux temperature overnight. After cooling down, the residue was washed with water, extracted with CH_2Cl_2, and organic layer was dried over Na_2SO_4. The solvent was evaporated to give **12b** as a yellow powder (190 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (s, 3H), 8.19 (d, J = 8.9 Hz, 3H), 8.00 (d, J = 8.9 Hz, 3H), 7.89 (d, J = 8.5 Hz, 3H), 7.72 (dt, J = 6.7, 1.3 Hz, 3H), 7.63 (d, J = 7.6 Hz, 3H), 7.52 (d, J = 7.6 Hz, 3H), 7.44 (t, J = 7.6 Hz, 3H), 7.25-7.19 (m, 6H), 7.07 (s, 3H), 6.68 (d, J = 7.4 Hz, 3H), 3.82 (d, J = 10.0 Hz, 3H), 3.44 (d, J = 14.0 Hz, 3H), 2.21-2.14 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.89, 148.32, 147.69, 140.67, 140.28, 136.50, 135.42, 132.61, 130.19, 129.51, 129.26, 128.78, 128.29, 127.40,

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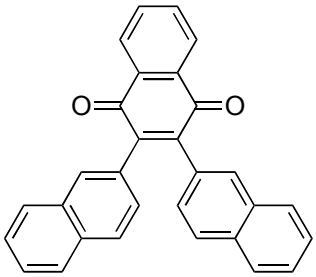
127.30, 126.81, 126.28, 125.78, 125.71, 122.97, 46.86, 36.67. HRMS-ESI+ *m/z* calcd for $C_{69}H_{46}N_3$ $[M+H]^+$ 916.3692, found 916.3692.

2.Synthesis of Starphene Derivatives

[2,2':3',2''-Terbenzobenzene]-1',4'-dione (31)



A mixture of 2,3-dibromo-1,4-naphthoquinone **29** (500 mg, 1.58 mmol), 2-naphthalene boronic acid **30** (654 mg, 3.80 mmol), $Pd(PPh_3)_4$ (95 mg, 0.08 mmol) and K_2CO_3 (1.31 g, 9.49 mmol) in degassed H_2O (1.6 mL, 50 equiv) and degassed toluene (20 mL), was heated at 120 ºC for 2 h under microwave irradiation. After the reaction mixture was cooled to room temperature, the solid was filtered through celite and washed with $CHCl_3$. The solvent was evaporated and the residue was cromatographed (SiO_2, 50% hexane/$CHCl_3$) to give **31** (621 mg, 95%) as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 5.7, 3.3 Hz, 2H), 7.83 (dd, *J* = 5.7, 3.3 Hz, 2H), 7.70-7.68 (m, 6H) 7.60 (d, *J* = 8.5 Hz, 2H), 7.44-7.38 (m, 4H), 7.16 (dd, *J* = 8.5, 1.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.76, 133.93, 132.80, 132.59, 132.26, 130.75, 130.65, 128.39, 127.82, 127.59, 127.25, 126.71, 126.64, 126.07.

Benzo[*c*]naphtho[1,2-*f*]tetraphene-11,16-dione (35)

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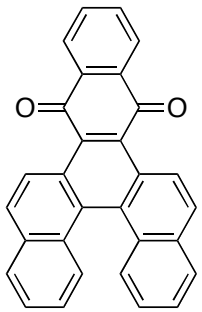
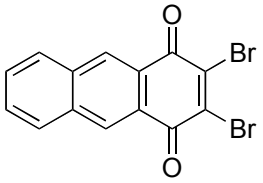


A solution of [2,2':3',2''-terbenzobenzene]-1',4'-dione **31** (54 mg, 0.13 mmol) and I_2 (2 mg, 0.007 mmol) in benzene (80 mL) was irradiated with 300 nm lamps for 3 h in the presence of air (O_2). The reaction mixture was washed with Na_2SO_3 (10%, 5 mL) and the organic layer was dried over $MgSO_4$. Solvent was evaporated to give **35** as a dark orange solid (53 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.34 (d, J = 9.4 Hz, 2H), 8.31-8.26 (m, 2H), 8.17 (d, J = 8.7 Hz, 2H), 8.08 (d, J = 9.2 Hz, 2H), 7.95 (d, J = 8.1 Hz, 2H), 7.83-7.78 (m, 2H), 7.56 (dt, J = 7.1, 0.9 Hz, 2H), 7.23 (dt, J = 7.2, 1.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.76, 134.31, 133.99, 133.10, 132.00, 130.56, 130.17, 129.94, 128.26, 128.19, 127.91, 127.77, 126.84, 125.43, 123.94.

2,3-Dibromoanthraquinone (33)



1,4-anthaquinone **33** (502 mg, 3.78 mmol) was stirred in glacial acetic acid (10 mL) and bromine (0.2 mL, 2.1 equiv, 7.8 mmol) was added dropwise. The mixture was stirred at room temperature for 30 min and refluxed for additional 3 h. After the reaction mixture was cooled to room temperature, was poured into ice water. The product was extracted with $CHCl_3$ and washed with $Na_2S_2O_4$, and water. The solvent was evaporated under reduced pressure to obtain 2,3-dibromo-1,4-atnraquinone (810 mg, 92%) as a brown solid. Pure product was obtained after recrystallization with $CHCl_3$. ^{1}H NMR

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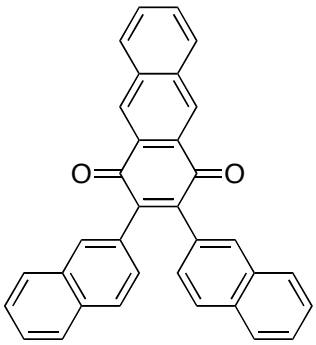
(400 MHz, $CDCl_3$) δ 8.73 (s, 2H), 8.10 (dd, J = 6.2, 3.2 Hz, 2H), 7.75 (dd, J = 6.4, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.64, 144.28, 134.92, 131.19, 130.38, 130.34, 126.66. HRMS-MALDI$^-$ *m/z* calcd for $C_{14}H_6Br_2O_2$ $[M]^-$ 363.8740, found 363.8756.

2,3-Di(naphthalen-2-yl)anthracene-1,4-dione (34)



A mixture of 2,3-dibromo-1,4-anthraquinone **33** (100 mg, 0.273 mmol), 2-naphthalene boronic acid **30** (113 mg, 0.656 mmol), $Pd(PPh_3)_4$ (16 mg, 0.014 mmol) and K_2CO_3 (226 mg, 1.64 mmol) in degassed H_2O (0.3 mL, 60 equiv) and degassed toluene (5 mL), was heated at 130 ºC for 1.5 h under microwave irradiation. After the reaction mixture was cooled to room temperature, the solid was filtered through celite and washed with $CHCl_3$. The solvent was evaporated and the residue was cromatographed (SiO_2, 50% hexane/$CHCl_3$) to give **34** (100 mg, 79%) as an orange solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 2H), 8.13 (dd, J = 6.2, 3.3 Hz, 2H), 7.74-7.69 (m, 8H), 7.62 (d, J = 8.5 Hz, 2H), 7.43-740 (m, 4H), 7.20 (dd, J = 8.5, 1.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.53, 147.32, 135.10, 132.80, 132.61, 130.99, 130.69, 130.23, 129.48, 129.04, 128.90, 128.41, 127.84, 127.60, 127.60, 127.23, 126.61, 126.04. LDI-MS calcd for $C_{34}H_{20}O_2$ $[M]^+$ 460.2, found 460.2

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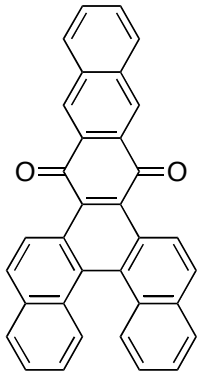
Dinaphtho[2,1-*a*:1',2'-*c*]tetracene-11,18-dione (36)



A solution of 2,3-di(naphthalen-2-yl)anthracene-1,4-dione **34** (18 mg, 0.039 mmol) and I_2 (0.01 mg, 0.025 mmol) in benzene (35 mL) was irradiated with 300 nm lamps for 3 h in the presence of air (O_2). The reaction mixture was washed with Na_2SO_3 (10%, 5 mL) and the organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was cromatographed (SiO_2, 40 to 60%, CH_2Cl_2/hexane) to give **36** as a dark orange solid (18 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (d, J = 9.2 Hz, 2H), 8.82 (s, 2H), 8.19 (d, J = 8.5 Hz, 2H), 8.13 (d, J = 6.3, 3.2 Hz, 2H), 8.11 (d, J = 9.1 Hz, 2H), 7.97 (d, J = 7.6 Hz, 2H), 7.70 (dd, J = 6.3, 3.2 Hz, 2H), 7.59-755 (m, 2H), 7.27-7.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 186.16, 135.26, 133.01, 131.86, 130.64, 130.19, 130.10, 129.99, 129.70, 129.31, 129.10, 128.79, 128.26, 128.01, 127.63, 125.26, 123.88. HRMS-ESI+ calcd for *m*/*z* $C_{34}H_{19}O_2Na$ $[M+Na]^+$ 481.1204, found 481.1204.

2,2'-(1,4-Dioxo-1,4-dihydronaphthalene-2,3-diyl)bis(anthracene-9,10-dione) (48)

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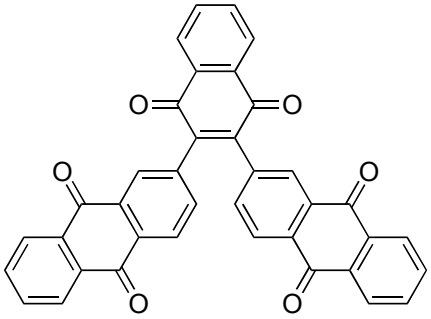
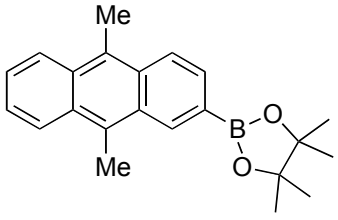


A mixture of 2,3-dibromo-1,4-naphthoquinone **29** (150 mg, 0.47 mmol), $PdCl_2$dppf (17 mg, 0.024 mmol), 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)anthracene-9,10-dione **47** (479 mg, 1.42 mmol) in degassed water (2.5 mL) and degassed toluene (5 mL) was heated at 100 ºC for 5 h. After the reaction mixture was cooled to room temperature, the solution was diluted with EtOAc, dried over $MgSO_4$ and the solvent was evaporated. The remaining solid was washed with hexane to recover unreacted **47** and subsequently purified by column chromatography (SiO_2, 1 to 5% EtOAc/CH_2Cl_2) to yield **48** as an orange solid (32 mg, 12%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28-8.22 (m, 6H), 8.19 (d, J = 8.1 Hz, 2H), 8.10 (d, J = 1.7 Hz, 2H), 7.90-7.86 (m, 2H), 7.79-7.74 (m, 4H), 7.55 (dd, J = 8.0, 1.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.58, 182.55, 182.40, 145.01, 138.67, 135.83, 134.64, 134.32, 133.47, 133.42, 133.16, 133.10, 131.89, 129.39, 127.40, 127.34, 127.10, 127.08. HRMS-ESI+ *m/z* calcd for $C_{38}H_{18}O_6Na$ $[M+Na]^+$ 593.1001, found: 593.1007.

2-(9,10-Dimethylanthracen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (51)



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A mixture of dimethylbromoanthracene **50**[284] (252 mg, 0.878 mmol), bispinacolatodiboron (317 mg, 1.23 mmol), $PdCl_2$dppf (3.2 mg, 0.044 mmol) and KOAc (174 mg, 1.75 mmol) in DMF (5 mL) was heated at 85 ºC for 15 h. After the reaction mixture was cooled to room temperature, the residue was filtered through celite and rinsed with hexane/EtOAc (10:1) until no more product was dissolved to eliminate excess of bispinacolate. The solvent was evaporated to give **51** (106 mg, 36%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.38- 8.31 (m, 2H), 8.29 (d, *J* = 8.9 Hz, 1H), 7.83 (dd, *J* = 8.9, 0.9 Hz, 1H), 7.56-7.49 (m, 2H), 3.18 (s, 3H), 3.09 (s, 3H), 1.42 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) 134.36, 130. 96, 130.61, 129.91, 129.87, 129.26, 128.62, 128.05, 125.58, 125.29, 125.15, 124.61, 124.23, 83.90, 24.96, 14.29, 14.07.

[284] Keana, J. F. W.; Prabhu, V. S.; Ohmiya, S.; Klopfenstein, C. E. *J. Org. Chem.* **1986**, *51*, 3456-3462.

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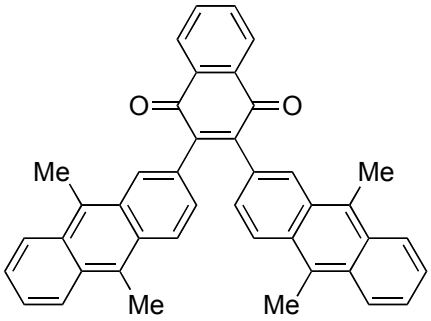
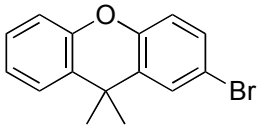
2,3-Bis(9,10-dimethylanthracen-2-yl)naphthalene-1,4-dione (53)



A mixture of 2,3-dibromo-1,4-naphthaquinone **29** (26.6 mg, 0.08 mmol), 9,10-dimethylanthraceneboronate **51** (51 mg, 0.15 mmol), $Pd(PPh_3)_4$ (20 mg, 0.02 mmol) and K_2CO_3 (71 mg, 0.45 mmol) in degassed H_2O (0.13 mL, 50 equiv) and degasses toluene (3 mL), was submitted to microwave irradiation at 140 ºC for 4 h. After the reaction mixture was cooled to room temperature, the solid was filtered through celite and washed with $CHCl_3$. The solvent was evaporated and the residue was cromatographed (SiO_2, 10 to 50% hexane/$CHCl_3$) to give **53** (15 mg, *ca.* 35%, not completely pure) as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, J = 5.8, 3.3 Hz, 2H), 8.24-8.21 (m, 4H), 8.20-8.16 (m, 2H), 8.12 (d, J = 9.2 Hz, 2H), 7.85 (dd, J = 5.7, 3.4 Hz, 2H), 7.47-7.42 (m, 4H), 7.31 (dd, J = 9.2, 0.9 Hz 2H), 2.95 (s, 3H), 2.79 (s, 3H).

2-Bromo-9,9-dimethyl-9*H*-xanthene (57)



9,9-Dimethyl xanthene **56** (500 mg, 2.38 mmol) was stirred in glacial acetic acid (30 mL) until it dissolved and bromine (0.07 mL, 0.6 equiv, 1.42 mmol) was added dropwise. The mixture was stirred at room temperature for 1.5 h and poured into an ice bath. The product was extracted with $CHCl_3$ and washed with $Na_2S_2O_4$ and H_2O. The organic layer was dried over Na_2SO_4 and the solvent was evaporated. The residue was

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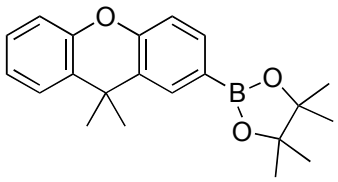
cromatographed (SiO_2, hexane) to give a 1:0.2 mixture of mono- (430 mg, *ca*. 49%) **57** and dibrominaed xanthene **58** products as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, for monobromoxanthene **57**) δ 7.50 (d, J = 2.3 Hz, 1H), 7.40 (dd, J = 7.8, 1.5 Hz, 1H), 7.29 (dd, J = 8.6, 2.4 Hz, 1H), 7.21 (m, 1H), 7.09 (td, J = 7.6, 1.2 Hz, 1H), 7.03 (dd, J = 8.1, 1.2 Hz, 1H), 6.94 (d, J = 8.6 Hz, 1H).

2-(9,9-Dimethyl-9*H*-xanthen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (59)



A mixture of **57** (252 mg, 0.865 mmol), bispinacolatodiboron (305 mg, 1.21 mmol), $PdCl_2$(dppp) (25.5 mg, 0.043 mmol) and KOAc (171 mg, 1.73 mmol) in DMF (6 mL) was heated at 85 ºC for 72 h. After the reaction mixture was cooled to room temperature, H_2O was added and the product was extracted with Et_2O. The combined organic extracts were dried over Mg_2SO_4, solvent was evaporated and the residue was cromatographed. (SiO_2, 0 to 20% EtOAc/hexane) to give **59** (110 mg, 38%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 1.4 Hz, 1H), 7.66 (dd, J = 7.6, 0.7 Hz, 1H), 7.41 (dd, J = 7.7, 1.6 Hz, 1H), 7.28 (m, 1H), 7.09-7.02 (m, 2H), 1.66 (s, 6H), 1.35 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$,) δ 152.85, 150.08, 134.23, 133.19, 130.37, 129.30, 127.31, 127.17, 126.18, 123.19, 116.34, 115.82, 83.67, 33.86, 32.57, 24.89. HRMS- APci+ *m/z* calcd for $C_{21}H_{26}BO_3$ $[M+H]^+$ 337.1975, found 337.1989.

2,3-Bis(9,9-dimethyl-9*H*-xanthen-2-yl)anthracene-1,4-dione (60)

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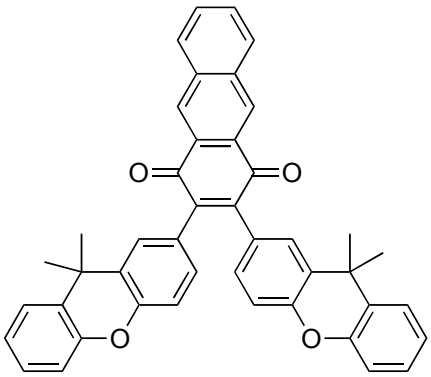
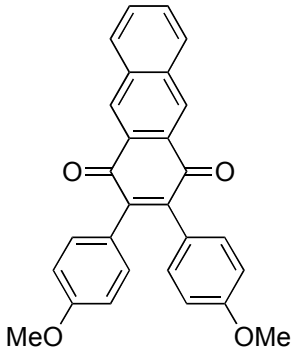


A mixture of 2-(9,9-Dimethyl-9*H*-xanthen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **59** (35,1 mg, 0.104 mmol), 2,3-dibromo-1,4-anthraquinone (**33**) (19,0 mg, 0.052 mmol), $Pd(Ph_3)_4$ (6 mg, 0,05 mmol) and K_2CO_3 (27 mg, 0.16 mmol) in degassed H_2O (46 µl, 2,6 mmol) and degassed toluene (2.5 mL) was heated at 140 ºC for 4 h under microwave irradiation. After the reaction mixture was cooled to room temperature, the solvent was evaporated and the residue cromatographed (SiO_2, 30 to 50% CH_2Cl_2/hexane) to give **60** (24 mg, 78%) as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 2H), 8.12 (dd, *J* = 6.2, 3.3 Hz, 2H), 7.71 (dd, *J* = 6.2, 3.2 Hz, 2H), 7.28 (dd, *J* = 7.8, 1.4 Hz, 2H), 7.19-7.12 (m, 4H), 7.08 (d, *J* = 2.0 Hz, 2H), 7.04-6.96 (m, 6H), 1.35 (s, 12H). HRMS-ESI+ *m/z* calcd for $C_{44}H_{32}O_4Na$ $[M+Na]^+$ 647.2198, found 647.2197.

2,3-Bis(4-methoxyphenyl)anthracene-1,4-dione (65)



A mixture of 4-metoxyphenylboronic acid (513 mg, 3.37 mmol), 2,3-dibromo-1,4-anthraquinone (**33**) (510 mg, 1.25 mmol), $Pd(PPh_3)_4$ (0.08 mg, 0.07 mmol) and K_2CO_3

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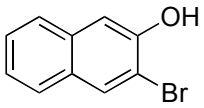
(1.17 g, 8.47 mmol) in degassed H_2O (1.2 mL, 54 equiv) and degassed toluene (18 mL), was heated at 120 ºC for 2 h under microwave irradiation. After the reaction mixture was cooled to room temperature, the solid was filtered through celite and washed with $CHCl_3$. The solvent was evaporated and the residue was cromatographed (SiO_2, 30 to 60% CH_2Cl_2/hexane) to give **65** as an orange solid (446 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.10 (dd, *J* = 6.2, 3.3 Hz, 1H), 7.69 (dd, *J* = 6.2, 3.2 Hz, 1H), 7.08 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.68, 159.39, 146.34, 135.01, 132.27, 130.34, 129.29, 128.96, 128.77, 126.03, 113.27, 55.19. HRMS-ESI+ *m/z* calcd for $C_{28}H_{20}O_4Na$ $[M+Na]^+$ 443.1259, found: 443.1269.

3-Bromo-2-naphthol (81)



Method A: A solution of 3-bromo-2-methoxynaphthalene **80** (10.0 g, 42.1 mmol) in AcOH (150 mL) and aqueous HBr (48%, 200 mL) was refluxed for 10 h. After the reaction mixture was cooled to room temperature, was diluted with water and extracted with CH_2Cl_2. The organic extracts were dried over Na_2SO_4, the solvent was evaporated and the residue was cromatographed (SiO_2, 10% EtOAc/hexane) to give **81** (6.0 g, 63%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.70-7.68 (m, 2H), 7.45 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.37 (s, 1H), 7.33 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 5.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.44, 134.04, 131.21, 129.49, 126.91, 126.77, 126.59, 124.48, 112.53, 110.71. HRMS-ESI$^-$ *m/z* calcd for $C_{10}H_7BrO$ $[M]^-$ 222.9582, found 222.9589.

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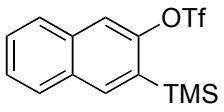
Method B:[285] To a solution of 3-bromo-2-methoxynaphthalene **80** (4.5 g, 19.0 mmol) in CH_2Cl_2 (600 mL) was added BBr_3 (100 mL, 100 mmol) at 0 ºC. The mixture was stirred at room temperature for 5 h. The excess of BBr_3 was decomposed by adding H_2O dropwise at 0 ºC. The organic layer was washed with water and brine, dried over Na_2SO_4 and the solvent was evaporate. The residue was cromatographed (SiO_2, 5% EtOAc/hexane) to give **81** as a white solid (3.1 g, 73%).

3-Trimethylsilylnaphthyl-2-trifluoromethanesulphonate (82)[286]



A mixture of 3-bromo-2-naphtol **81** (2.92 g, 14.2 mmol) and HMDS (5.9 mL, 31.2mmol) in THF (50 mL) was stirred under refluxed for 90 min in a flask provided with a condenser and a $CaCl_2$ tube. The solvent was evaporated under reduced pressure and the residue was subjected to vacuum. Sylylether crude was dissolved in THF (100 mL), the solution was cooled to -100 ºC, and *n*-BuLi (5.7 mL, 15.6 mmol) was added dropwise. The mixture was stirred until temperature reached -80 ºC and then the mixture was again cooled to -100 ºC. Tf_2O (4.95 g, 17.0 mmol) was added dropwise and stirring was continued until the temperature reached -80 ºC. Cold sat aq. $NaHCO_3$ was added, the phases were separated and the aqueous layer was extracted with ether. Combined organic extracts were dried over Mg_2SO_4 and the solvent was evaporated. The residue was cromatographed (SiO_2, hexane) to give **82** (3.08 g, 68%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.89-7.84 (m, 2H), 7.80 (s, 1H), 7.58-7.52 (m, 2H), 0.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.55, 137.53, 134.11, 131.80, 131.06, 127.95, 127.77, 127.76, 126.94, 118,59 (q, J = 320.2 Hz), 116.48, -0.72.

285 According to: Lingenfeller, D. S.; Helgenson R. C.; Cram, D. J. *J. Org. Chem.*, **1981**, *46*, 393-406.

286 According to: Peña, D.; Cobas, A.; Pérez, D.; Guitán, E. *Synthesis* **2002**, 1454-1458.

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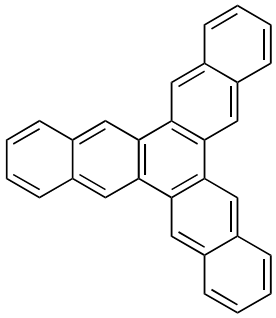
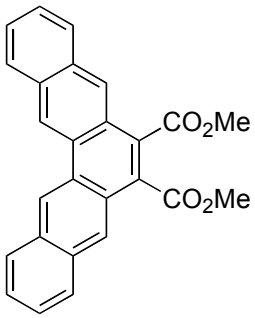
Trinaphthalene (73)[286]



A solution of **82** (202 mg, 1.03 mmol) in CH_3CN (4 mL) was added to a suspension of Bu_4NF (1M in THF, 1.03 mL, 1.03 mmol) and $Pd(PPh_3)_4$ (0.06 mg, 0.05 mmol) in dry CH_3CN (2 mL) and the solution was stirred at room temperature for 12 h. The solid precipitate was collected by filtration and washed successively with CH_3CN and CH_2Cl_2 and dried under vacuum to give **73** (30 mg, 41%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 6H), 8.10 (dd, J = 6.3, 3.2 Hz, 6H), 7.58 (dd, J = 6.3, 3.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.85, 129.01, 128.12, 126.40, 122.68. HRMS-MALDI+ *m/z* calcd for $C_{30}H_{18}$ $[M]^+$ 378.1403, found 378.1406.

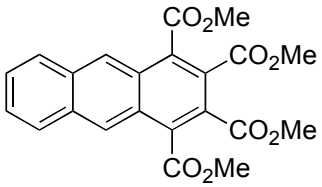
Dimethyl penthaphene-6,7-dicarboxylate (83)



A solution of the 3-trimethylsilylnaphthyl-2-trifluoromethanesulphonate **82** (201 mg, 0.574 mmol) in CH_3CN (5 mL) was added to a suspension of CsF_2 (176 mg, 1.15 mmol), DMAD (98 mg, 0.69 mmol), $Pd(OAc)_2$ (13 mg, 0.058 mmol) and

PPh_3 (4.5 mg, 0.17 mmol) in CH_3CN (5 mL). The mixture was stirred under argon at room temperature for 20 h. The solvent was evaporated and the residue was cromatographed (SiO_2, 20 to 40% CH_2Cl_2/hexane) to give **83** (55 mg, 49%) as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 9.27 (s, 2H), 8.57 (s, 2H), 8.15 (d, J = 8.2 Hz, 2H), 8.04 (d, J = 8.2 Hz, 2H), 7.61 (m, 4H), 4.11 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.30, 132.81, 132.26, 130.64, 128.70, 128.55, 128.16, 127.28, 126.86, 126.55, 125.14, 122.26, 52.89. HRMS-ESI+ *m/z* calcd for $C_{26}H_{18}O_4Na$ $[M+Na]^+$ 417.1103, found 417.1118.

Tetramethyl anthracene-1,2,3,4-tetracarboxylate (84)[287,288]



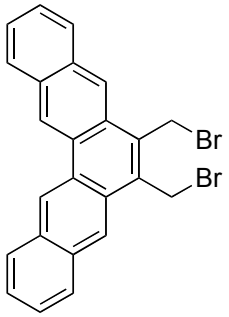
A solution of the 3-trimethylsilylnaphthyl-2-trifluoromethanesulphonate **82** (503 g, 1.43 mmol) in CH_3CN (15 mL) was added to a suspension of CsF_2 (440 mg, 2.87 mmol), DMAD (1.02 g, 7.17 mmol) and $[Pd_2(dba)_3]$ (74 g, 0.071 mmol) in CH_3CN (15 mL). The mixture was stirred under argon at room temperature for 36 h. The solvent was evaporated and the residue cromatographed (SiO_2, 40% EtOAc/hexane) to give **96** (391 mg, 66%) as a bright yellow solid. mp 128-134 ºC. ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (s, 2H), 8.06 (dd, J = 6.5, 3.3 Hz, 2H), 7.60 (dd, J = 6.5, 3.2 Hz, 2H), 4.09 (s, 6H), 3.94 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.42, 166.74, 134.61, 133.27, 128.61, 127.85, 126.66, 126.34, 126.14, 53.24, 53.14. HRMS-ESI+ *m/z* calcd for $C_{22}H_{18}O_8Na$ $[M+Na]^+$ 433.0899, found 433.0914.

6,7-Di(bromomethyl)penthaphene (86)

287 According to: Peña, D.; Pérez, D.; Guitán E.; Castedo, L. *J. Org. Chem* **2000**, *65*, 6944-6950.

288 Product described in: Bennett, M. A.; Hockless D. C. R.; Wegner, E. *Organometallics* **1985**, *14*, 2091-2101.

ISBN:978-84-693-4592-4/DL:T.1005-2010



$LiAlH_4$ (42 mg, 1.1 mmol) was added to THF (2 mL) and cooled to 0 ºC. To the suspension was added dropwise a solution of dimethyl pentaphene-6,7-dicarboxylate (**83**) (200 mg, 0.507 mmol) in THF (3 mL) for 15 min. The mixture was warmed to room temperature and stirred for 1 h. After cooling to 0 ºC, to the mixture was added a drop of water (50 μL), a few drops of NaOH (15 %) (50 μL) a few drops of water (150 μL) and dried over Na_2SO_4. The precipitate was filtered off and the residue was evaporated under reduced pressure to give the corresponding tetraol (**85**), which was used without further purification.

The solid was dissolved in 1,2-dichloroethane (3 mL), treated with phosphorus tribromide (141 mg, 0.521 mmol), and stirred at room temperature for 1 h. The mixture was quenched with water and extracted with $CHCl_3$. The combined organic extracts were washed with brine and dried over Na_2SO_4. The solvent was evaporated and the residue was dissolved in $CHCl_3$ (2 mL) and it was poured to MeOH (10 mL). The resulting yellow precipitate was collected by filtration and dried under vacuum to obtain 158 mg (68% yield calculated by NMR) of not completely pure product **86** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 2H), 8.63 (s, 2H), 8.15 (m, 4H), 7.62 (m, 4H), 5.18 (s, 4H).

1,2,3,4-Tetrakis(bromomethyl)anthracene (88)

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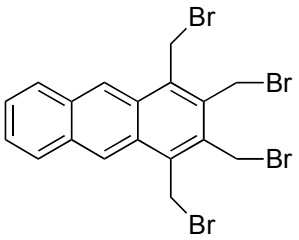

$LiAlH_4$ (148 mg, 3.90 mmol) was added to THF (10 mL) and cooled to 0 ºC. To the suspension was added dropwise a solution of tetra(methoxycarbonyl)anthracene (402 mg, 0.975 mmol) in THF (12 ml) for 15 min. The mixture was warmed to room temperature and stirred for 1 h. After cooling to 0 ºC, to the mixture was added a drop of water (150 μL), a few drops of NaOH (15%) (150 μL) a few drops of water (450 μL) and dried (Na_2SO_4). The precipitate was filtered off and the residue was evaporated under reduced pressure to give the corresponding tetra-alcohol **87**, which was used without further purification.

Tetraol **87** was dissolved in 1,2-dichloroethane (15 mL), treated with phosphorus tribromide (251 mg, 0.926 mmol) and stirred at room temperature for 1 h. The mixture was quenched with water and extracted with $CHCl_3$. The combined organic phase was washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was dissolved in $CHCl_3$ (2 mL) and it was poured to MeOH (10 mL). The resulting yellow precipitate was collected by filtration and dried to give 31 mg (10%, for the two steps, calculated by NMR) of not completely pure **100** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 2H), 8.10 (dd, J = 6.4, 3.3 Hz, 2H), 7.59 (dd, J = 6.5, 3.3 Hz, 2H), 5,18, (s, 4H), 4.96 (s, 4H).

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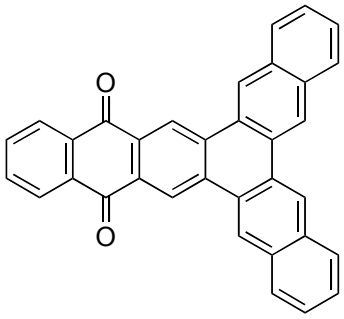
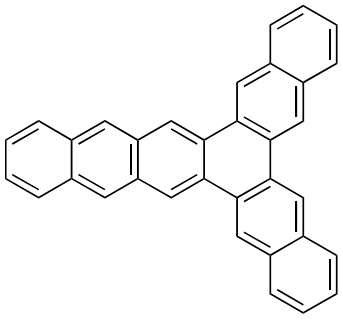
Benzo[*b*]trinaphthylene-13,18-dione (95)



6,7-di(bromomethyl)penthaphene **86** (31 mg, 0.043 mmol), 1,4 naphthoquinone (10 mg, 0.063 mmol) and KI (72 mg, 0.43 mmol), were dissolved in dry DMF (4.5 mL) and stirred at 110 ºC for 16 h. The reaction mixture was cooled to room temperature, filtered and washed with CH_2Cl_2. The solid was then stirred in an Erlenmeyer with water to remove excess of KI and filtered once again, washed with aecetone and CH_2Cl_2 to give **95** (72 mg, 74%) as an insoluble orange solid. ^{1}H NMR (500 MHz, $Cl_2CDCDCl_2$, 403 K) δ 9.48 (s, 2H), 9.12 (s, 2H), 9.07(s, 2H), 8.38 (dd, *J* = 5.8, 3.3 Hz, 2H), 8.09-8.02 (m, 4H), 7.75 (dd, *J* = 5.8, 3.3 Hz, 2H), 7.56 (m, 4H). MALDI+ (DCTB) *m/z* calcd for $C_{34}H_{18}O_2$ [M]+ 458.1, found: 458.1.

Benzo[*b*]trinaphthylene (96)



$LiAlH_4$ (4.1 mg, 0.11 mmol) was added to a ice-cooled suspension of benzo[*b*]trinaphthylene-13,18-dione **95** (10.0 mg g, 0.027 mmol) in dry THF (3 mL) under argon atmosphere and was refluxed for 1 h. After the reaction mixture was cooled

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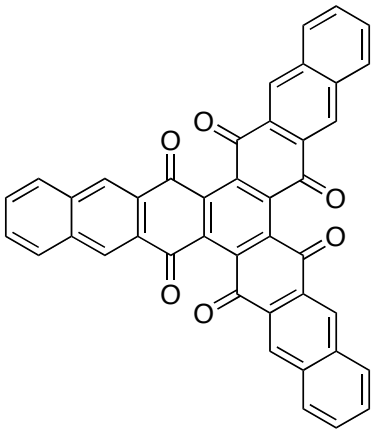
to room temperature, HCl (6 M, 22 μL) was added at 0 ºC on an ice bath. The mixture was then refluxed for additional 3 h. The residue was filtered, washed with H_2O, CH_2Cl_2, MeOH and Et_2O. After drying, the residue was treated again with LiAlH4 (4.1 mg, 0.11 mmol) and HCl (6 M, 22 μL) following the same procedure to give a mixture of compounds. The residue was cromatographed to give analytical sample of **96** as the major compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (s, 2H), 9.12 (s, 2H), 9.06 (s, 2H), 8.68 (s, 2H), 8.10-7.99 (m, 6H), 7.59-7.56 (m, 6H).

Cyclo-tri-1,4-anthraquinone (104)[289]



1,4-Anthraquinone **(99**) (50 mg, 0.24 mmol) was dissolved in Et_2O (10 mL) and stirred with $Na_2S_2O_4$ (6% aqueous solution, 7.5 mL) for 30 min. The organic layer was separated, dried over Na_2SO_4 and the solvent evaporated under nitrogen atmosphere. The remaining 1,4-dihydroxyanthracene (**103)** was dissolved in degassed pyridine (100 mL) and 1,4-anthraquinone (5.00 g, 24.0 mmol) was added. The mixture was stirred for 40 h at room temperature and the precipitate was filtered off and was washed with pyridine (20 mL) and $CHCl_3$ (250 mL) to give **104** as a green-yellow solid (1.73 g, 35 %). ^{1}H NMR (500 MHz, $Cl_2CDCDCl_2$, 403 K) δ 8,61 (m, 6H), 8.05 (m, 6H), 7.69

289 According to: H. Brockmann and H. Laatsch, *Chem. Ber.*, **1973**, *106*, 2058-2069.

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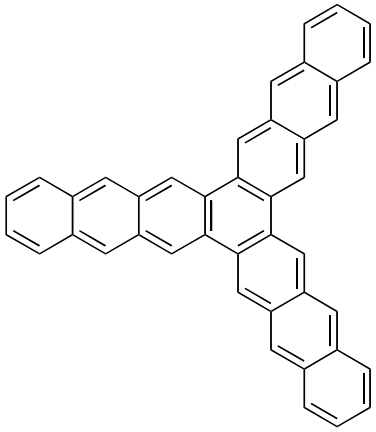
(m, 6H). HR-MALDI+ (dithranol) *m/z* calcd for $C_{42}H_{19}O_6$ $[M+H]^+$ 619.1176, found 619.1205.

Decastarphene-(3.3.3) (97)



$LiAlH_4$ (150 mg, 3.90 mmol) was added to an ice-cooled suspension of *cyclo*-tri-1,4-anthraquinone **104** (200 mg, 0.320 mmol) in dry THF (10 mL) under argon atmosphere and refluxed for 1 h. After cooling down to 0 ºC, HCl (6 M, 2.42 mL) was added and the reaction was refluxed for 5 additional hours. After cooling down, the residue was filtered off and the precipitate was washed with H_2O (3 x 5 mL), MeOH (3 x 5 mL), CH_2Cl_2 (2 x 5 mL) and Et_2O (2 x 5 mL). After drying, the residue was treated again with LiAlH4 (150 mg, 3.90 mmol) and HCl (6 M, 2.42 mL) following the same procedure to give **97** as a yellow/brown highly insoluble solid (30 mg, 18 %) (R_f = 0.98, $CHCl_3$, green fluorescent). ^{1}H NMR (500 MHz, $Cl_2CDCDCl_2$, 403 K) δ 9.17 (s, 6H), 8.61 (s, 6H), 8.03 (dd, *J* = 5.4, 3.3 Hz, 6H), 8.46 (dd, *J* = 5.5, 3.3 Hz, 6H). HR-MALDI+ (dithranol) *m/z* calcd for $C_{42}H_{24}$ $[M]^+$ 525.1872, found 525.1868.

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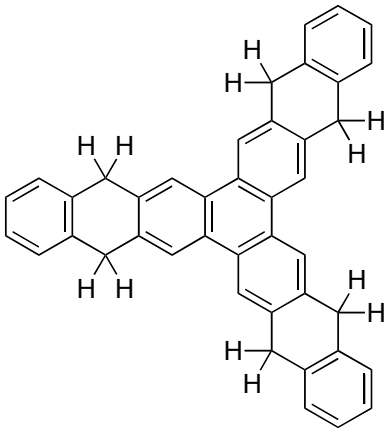
5,8,13,16,21,24-Hexahydrodecastarphene-(3.3.3) (105)



Red phosphorous (500 mg, 16.1 mmol) and *cyclo*-tri-1,4-anthraquinone **104** (500 mg, 0.808 mmol) in HI (57% in water, 10 mL) were heated at 200 ºC for 2 h in a pressure vessel. After cooling down to room temperature the reaction mixture was filtered off and the precipitate was washed with H_2O (3 x 10 mL) and MeOH (3 x 10 mL). The remaining solid was extracted for 24 h with benzene using a Soxhlet extractor system. After evaporation of the filtrate a brown solid was obtained (350 mg), mainly consisting of **105** (80%) according to spectroscopic NMR and IR data. An analytically pure sample was obtained by column chromatography on Al_2O_3 using $CHCl_3$ as eluent. The first fractions containing mainly the blue-fluorescent product (Rf = 1, $CHCl_3$, blue fluorescent) were evaporated and the remaining solid was dissolved in a minimum quantity of CH_2Cl_2 and precipitated by addition of an excess of hexane. The precipitate was filtered off and washed with hexane and cold CH_2Cl_2 to afford pure sample of **105**. ^{1}H NMR (400 MHz, $Cl_2CDCDCl_2$) δ 8,48 (s, 6H), 7,34 (dd, J = 5.4, 3.3 Hz, 6H), 7.19 (dd, J = 5.5, 3.3 Hz, 6H), 4.15 (s, 12H); ^{13}C NMR (100 MHz, $Cl_2CDCDCl_2$) δ 136.28, 135.40, 127.43, 127.05, 125.85, 121.01, 36.09.

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Decastarphene-(3.3.3) (97).

Aromatization

Method A: 5,8,13,16,21,24-Hexahydrodecastarphene-(3.3.3) **105** (150 mg, 0.280 mmol) and chloranil (450 mg, 1.81 mmol) were refluxed in a mixture of 1,2-dichlorobenzene/HOAc glacial 3:1, 60 mL) for 3 h. The mixture was concentrated and the residue was washed with toluene (50 mL) and $CHCl_3$ (20 mL) to remove excess of chloranil and other byproducts. The mixture was filtered over silica and washed with toluene (200 mL). The silica containing the product was extracted for 24 h with $CHCl_3$ using a Soxhlet extractor system. After evaporation of the solvent, product **109** was obtained after recrystalization in *p*-xylene (15 mg, 10%).

Method B*:* A mixture of 5,8,13,16,21,24-Hexahydrodecastarphene-(3.3.3) **105** (200 mg, 0.370 mmol) and Pd (10 wt% on carbon, 300 mg, 0.282 mmol) in xylene was refluxed for 3 days under N_2 atmosphere. The mixture was filtered off and the product was extracted 48 h with $CHCl_3$ using a Soxhlet extractor system. The product was obtained after recrystalization in $CHCl_3$ (18 mg, 80 % purity).

3. Azastarphenes

The synthesis of 2,2'-(1,2-phenylene)diacetonitrile,[290] and benzene-1,2-diamine[291] have already been described.

Diquinoxalino[2,3-*a*:2',3'-*c*]phenazine (113)[292]

290 Albano, G.; Belser, P.; De Cola, L.; Gandolfi, M. T. *Chem. Commun.***1999**,1171-1172.

291 Dupureur, C. M.; Barton, J. K. *Inorg. Chem.* **1997**, *36*, 33-43.

292 Barlow, S.; Zhang,Q.; Kaafarani, B. R.; Risko, C.; Amy, F.; Chan, C. K.; Domercq, B.; Starikova, Z. A.; Antipin, M. Y. Timofeeva, T.V.; Kippelen, B.; Brédas, J.-L.; Kahn, A.; Marder, S. R. *Chem. Eur. J.* **2007**, *13*, 3537-3547.

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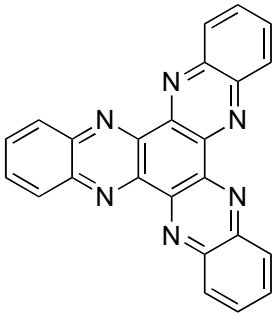
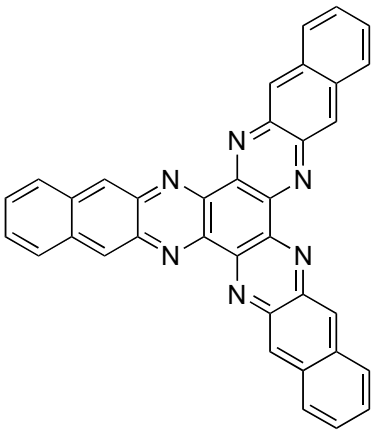


A mixture of hexaketocyclohexane octahydratate (100 mg, 0.311 mmol) and 1,2-diaminobenzene (140 mg, 1.29 mmol) in degassed acetic acid (20 mL) was heated at 100 ºC for 16 h under nitrogen atmosphere. After the reaction mixture was cooled to room temperature, the solid was collected by filtration and washed with hot acetic acid that was recrystalized with $CHCl_3$/hexane to give **113** as a yellow solid (110 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (dd, J = 6.5, 3.4 Hz, 6H), 8.06 (dd, J = 6.5, 3.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.59, 143.56, 132.29, 130.67. LDI$^+$ *m/z* calcd for $C_{24}H_{13}N_6$ $[M+H]^+$ 385.1196, found 385.1198.

Azadecastarphene-(3.3.3) (115)



A mixture of hexaketocyclohexane octahydratate (**111**) (100 mg, 0.311 mmol) and 1,2-diaminonaphthalene (**114**) (205 mg, 1.30 mmol) in degassed acetic acid (30 mL) was heated at 100 ºC for 16 h under nitrogen atmosphere. After the reaction mixture was cooled to room temperature, the solid was collected by filtration and washed with hot acetic acid that was recrystalized with $CHCl_3$ to give **115** as a red solid (138 mg, 83%).

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^{1}H NMR (500 MHz, $Cl_2CDCDCl_2$, 403 K) δ 9.16 (bs, 6H) 8.19 (bs, 6H), 7.62 (bs, 6H); HR-LDI$^+$ *m/z* calcd for $C_{36}H_{19}N_6$ $[M+H]^+$ 535.1666, found 535.1653.

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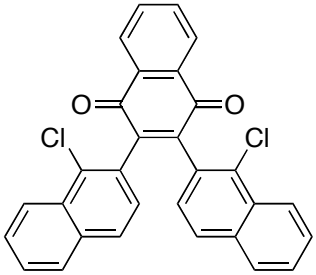
4. Additional Compounds

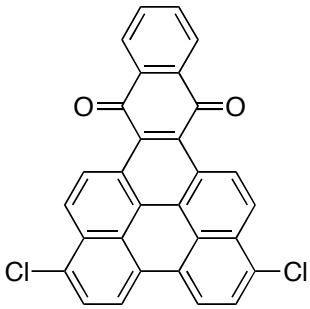
The following compounds could not be isolated completely pure but could be tentatively assigned by 1H NMR or Mass spectrometry.

1,1''-dichloro-[2,2':3',2''-terbenzobenzene]-1',4'-dione (45)



Dinaphthoquinone **31** (50.3 mg, 0.122 mmol) was dissolved in CH_2Cl_2 (50 mL), the solution was then degassed by bubbling with argon for 30 min. $FeCl_3$ (119 mg, 0.734 mmol) in CH_3NO_2 (0.5 mL) was added dropwise. The reaction was stirred at room temperature for 1 h. MeOH (50 mL) was added. Solvent was concentrated, and precipitate was filtered off and washed with MeOH to give **45** as a red solid not completely pure (45 mg, *ca.* 77%) ^{1}H NMR (400 MHz, $CDCl_3$) 8.68 (dd, J = 6.2, 3.2 Hz, 2H), 8.63 (d, J = 8.2 Hz, 2H), 8.54 (d, J = 8.6 Hz, 2H), 8.06 (d, J = 8.1 Hz, 2H), 7.92 (d, J = 8.6 Hz, 2H), 7.78- 7.68 (m, 4H), 7.62 (t, J = 7.4 Hz, 2H).

1,6-Dichloroanthra[1,2,3,4-*ghi*]perylene-9,14-dione (39)



Benzo[*c*]naphtho[1,2-*f*]tetraphene-11,16-dione **35** (20.1 mg, 0.049 mmol) was dissolved in CH_2Cl_2 (30 mL), the solution was then degassed by bubbling with argon for 30 min.

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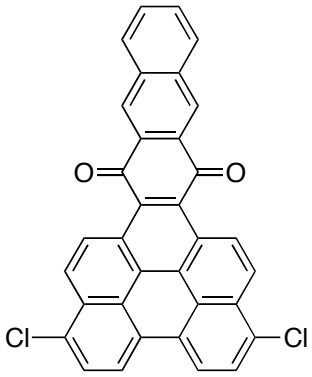
$FeCl_3$ (143 mg, 0.882 mmol) in CH_3NO_2 (0.2 mL) was added dropwise. The reaction was stirred at room temperature for 3 h. MeOH (30 mL) was added. Solvent was concentrated, and precipitate was filtered off and washed with MeOH to give a mixture of oxidative dehydrogenation compound **x** together with mono- di- and tri-chlorinated compounds according to mass spectrometry. Dichlorinated compound **39** could be detected and analyzed by 2D 1H NMR analysis at high temperature. ^{1}H NMR (500 MHz, $Cl_2CDCDCl_2$, 403 K) δ 9.73 (d, J = 9.7 Hz, 2H), 8.79 (d, J = 8.5 Hz, 2H), 8.61 (d, J = 9.7 Hz, 2H), 8.30 (dd, J = 5.7, 3.3 Hz, 2H), 8.09 (d, J = 8.4 Hz, 2H), 7.80 (dd, J = 5.8, 3.2 Hz, 2H). LDI$^+$ *m/z* 406.1 ($C_{30}H_{14}O_2$), 440.1 ($C_{30}H_{13}ClO_2$), 474.1 ($C_{30}H_{12}Cl_2O_2$) and 508.1 ($C_{30}H_{11}Cl_3O_2$).

1,6-Dichlorodinaphtho[8,1,2-*cde*:2',1',8'-*uva*]pentacene-9,16-dione (40)



Dinaphtho[2,1-*a*:1',2'-*c*]tetracene-11,18-dione **36** (11 mg, 0.033 mmol) was dissolved in CH_2Cl_2 (20 mL), the solution was then degassed by bubbling with argon for 30 min. $FeCl_3$ (80 mg, 0.49 mmol) in CH_3NO_2 (0.2 mL) was added dropwise. The reaction was stirred at room temperature for 1 h. MeOH (30 mL) was added. Solvent was concentrated, and precipitate was filtered off and washed with MeOH to give a mixture of oxidative dehydrogenation compound **38** together with mono- and di-chlorinated compounds according to mass spectrometry. Dichlorinated compound **39** could be detected and analyzed by 2D ^{1}H NMR análisis. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (d, J = 9.4 Hz, 2H), 9.02 (d, J = 7.6 Hz, 2H), 8.77 (s, 1H), 8.24-8.17 (m, 2H), 8.10-8.07 (m,

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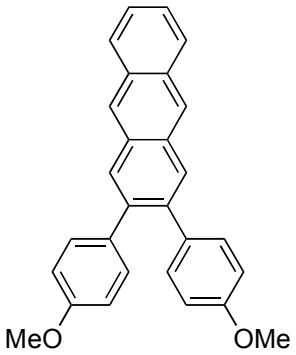
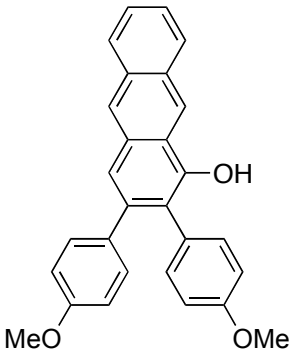
2H), 7.66 (dd, J = 5.7, 3.3 Hz, 2H), 7.48 (dd, J = 5.7, 3.3 Hz, 2H). LDI$^+$ *m/z* 456.1 ($C_{34}H_{16}O_2$), 490.1 ($C_{34}H_{15}ClO_2$), 526.1 ($C_{34}H_{14}Cl_2O_2$) and 508.1 ($C_{30}H_{11}Cl_3O_2$).

2,3-Bis(4-methoxyphenyl)anthracene (67)

2,3-Bis(4-methoxyphenyl)anthracen-1-ol (68)



67



68

$LiAlH_4$ (64.7 mg, 1.71 mmol) was added to an ice-cooled suspension of 2,3-bis(4-methoxyphenyl)anthracene-1,4-dione (**65**) (120 mg, 0.328 mmol) in dry THF (8 mL) under argon atmosphere and refluxed for 1 h. After cooling down to 0 ºC, HCl (6 M, 3.2 mL) was added and the reaction was refluxed for 3 additional hours. After cooling down, the residue was filtered off and the precipitate was washed with H_2O (3 x 8 mL), MeOH (3 x 8 mL), CH_2Cl_2 (2 x 8 mL) and Et_2O (2 x 8 mL). After drying, the residue was treated again with $LiAlH_4$ (64.7 mg, 1.71 mmol) and HCl (6 M, 3.2 mL) following the same procedure. The residue was cromatographed (SiO_2, 20 to 80 %, CH_2Cl_2/hezane) to give **67** not completely as mayor product (28 mg, *ca*. 21%) and hydroxy intermediate **68 (45 mg, 17%)**. ^{1}H NMR (400 MHz, $CDCl_3$, for **67**) δ 8.43 (s, 2H), 8.01-7.99 (m, 4H), 7.45 (dd, J = 6.6, 3.2 Hz, 2H), 7.19 (d, J = 8.8 Hz, 4H), 6.82 (d, J = 8.8 Hz, 4H), 3.82 (s, 6H). ^{1}H NMR (400 MHz, $CDCl_3$, for **68**) δ 8.84 (s, 1H), 8.38 (s, 1H), 8.07-8.04 (m, 1H), 8.00-7.98 (m, 1H), 7.63 (s, 1H), 7.51-7.40 (m, 2H), 7.17 (d, J = 8.7 Hz, 1H), 7.11 (d, J = 8.7 Hz, 1H), 6.92 (d, J = 8.7 Hz, 1H), 6.75 (d, J = 8.8 Hz, 1H), 5.87 (s, 1H), 3.83 (s, 3H), 3.78 (s, 3H).

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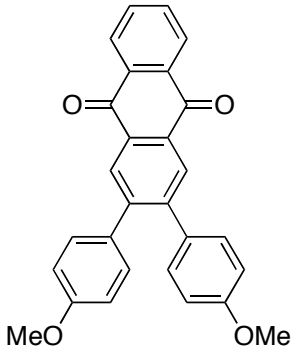
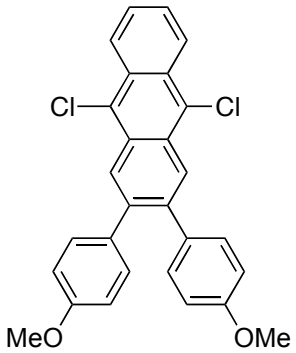
2,3-Bis(4-methoxyphenyl)anthracene-9,10-dione (69a)



A solution of 2,3-bis(4-Methoxyphenyl)anthracene **(67)** (25 mg, 0.064 mmol) and I_2 (0.01 mg, 0.023 mmol) in benzene (40 mL) was irradiated with 300 nm lamps for 3 h in the presence of air (O_2). The reaction mixture was washed with Na_2SO_3 (10%, 5 mL) and the organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was cromatographed (SiO_2, 40 to 60%, CH_2Cl_2/hexane) to give **69a** as a dark orange solid (18 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (dd, J = 5.8, 3.3 Hz, 2H), 8.32 (s, 2H), 7.81 (dd, J = 5.8, 3.3 Hz, 2H), 7.16 (d, J = 8.8 Hz, 4H), 6.83 (d, J = 8.8 Hz, 2H), 3.82 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 183.10, 159.21, 145.95, 134.04, 133.78, 132.16, 131.93, 130.87, 129.54, 127.22, 113.77, 55.26. HRMS-ESI+ calcd for *m/z* $C_{28}H_{20}O_4Na$ $[M+Na]^+$ 443.1259, found 443.1259.

9,10-Dichloro-2,3-bis(4-methoxyphenyl)anthracene 69b



2,3-bis(4-Methoxyphenyl)anthracene **(67)** (24 mg, 0.06 mmol) was dissolved in CH_2Cl_2 (20 mL), the solution was then degassed by bubbling with argon for 30 min. $FeCl_3$

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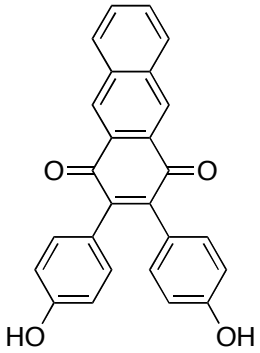
(128 mg, 0.770 mmol) in CH_3NO_2 (0.3 mL) was added dropwise. The reaction was stirred at room temperature for 1 h. MeOH (20 mL) was added. Solvent was concentrated, and precipitate was filtered off and washed with MeOH to give dichlorinated compound **69b**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (dd, *J* = 6.8, 3.2 Hz, 2H), 8.50 (s, 2H), 7.62 (dd, *J* = 6.8, 3.2 Hz, 2H), 7.22 (d, *J* = 8.7 Hz, 4H), 6.84 (d, *J* = 8.7 Hz, 4H), 3.82 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 158.82, 140.48, 133.26, 131.06, 129.28, 128.47, 127.83, 126.98, 126.22, 125.17, 113.54, 55.26.

2,3-bis(4-hydroxyphenyl)anthracene-1,4-dione (69c)



BBr_3 (1M in CH_2Cl_2, 2.70 mL, 2.70 mmol) was added at 0 ºC to a solution of 2,3-bis(4-methoxyphenyl)anthracene-1,4-dione (**65**) (0.99 mg, 0.27 mmol) in CH_2Cl_2 (20 mL) and stirred at room for X h. Dropwise addtion of H2O (10 mL) to decompose excess of BBr_3. The organic layr was washed with water, dried (Mg_2SO_4) and the solvent was evaporated. The residue was cromatgraphedto to give an inseparable mixture of **69c** and mono and di- bromo compounds according to mass spectrometry. ^{1}H NMR (400 MHz, $CDCl_3$, for **69c**) δ 8.71 (s, 2H), 8.10 (dd, *J* = 6.1, 3.4 Hz, 2H), 7.70 (dd, *J* = 6.2, 3.2 Hz, 1H), 7.02 (d, *J* = 8.7 Hz, 4H), 6.73 (d, *J* = 8.5 Hz, 4H), 5.05 (s, 2H). ESI$^+$ *m/z* 493.0 ($C_{26}H_{15}BrO_4Na$), 572.9 ($C_{26}H_{14}Br_2O_4Na$)

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